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Different Philosophies of Genetics*

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Prudens quaestio quasi dimidium scientiae.

IN the United States, a presidential address is usually scheduled for delivery after a banquet. Probably the underlying idea is that a well-fed audience is in a pleasant and mild mood, not too attentive, not too critical, and ready to submit quietly for an hour to whatever the old man is willing to produce. Unfortunately, I am not in this pleasant position today, having to face a hungry audience (at least mentally so), full of zeal, and with sharpened critical faculties. I might even quote here from Aristophanes (*The Clouds*):

> Phidippides: What do they call themselves?
> Strepsiades: I do not know exactly but they are deep thinkers and most admirable people.

Knowing this to be the case, I had to solve the difficult problem of deciding upon a topic worthy of my audience.

This means a topic which is not so special that it interests only a small group, but which nevertheless is on a sufficiently technical level; one which is general but not so general that it becomes commonplace; one which is to a certain extent controversial, at least sufficiently so to make an interesting discussion, yet at the same time is not so controversial that it is unsuitable for a discussion without the use of the gentle art of making enemies; one which is based upon the performance of the past without being of yesterday and retrospective, but also one which dares to look into the future and to risk a jump beyond the present without soaring into a flight of pure imagination; finally, it means a topic the discussion of which has a personal, subjective angle based upon the speaker's scientific past, but which does not end in dogmatism and opinionation.

Just as is the case with other sciences, for example, physics, so also genetics is based upon what a theoretical physicist (Sir E. Whittaker) has called "the unchangeable brute facts of experience which have the character of permanence." But, continuing the quotation, "The situation is different with an intellectual adventure such as theoretical physics; it is built around conceptions and the progress of the subject consists very largely in replacing these conceptions by other conceptions, which transcend or even contradict them."

There is no historically recognized science of theoretical genetics comparable to theoretical physics or natural philosophy, as it is called in England. But each thinking geneticist, in interpreting his factual data and in trying to fit his results into the total theoretical structure of his science, does it under the conscious or subconscious influence of his basic philosophy or *Weltanschauung* in regard to genetical thought. I mean to say by this that, when we interrupt our experiments to do some constructive thinking, we are likely to draw frequently widely divergent conclusions from the same facts. It is not that the facts are ambiguous or insufficiently established; is is the way we are looking at the facts that is different. But this difference does not necessarily mean that one is a better thinker than another. Rather it means, in many cases, that the general way of thinking, of analyzing facts and of putting them into categories, is different in different minds.

There is no objective way to decide which is the correct mental attitude and which is not. The decision lies with time, which as often as not will decide that both attitudes were wrong and will replace them by a third and a fourth, again subject to selection as further facts allow new evaluation of ideas in time. It is obvious, as was already hinted by the use of the word *selection*, that just this competition of divergent ideas, even basically, philosophically divergent ideas, is the method by which the theoretical level of a science develops.

Genetics is not any exception and, therefore, I should like to inquire into what I believe to be the two basic divergent philosophies of our science and to confront them with each other. Nobody would expect other than that in so doing I cannot help arguing in favor of my own way of looking at things. But this does not mean that I take less seriously the opposed points of view of some great geneticists and thinkers with whom I have to disagree. I realize well that another, in the same place, might argue quite differently. Although I am convinced of the correctness of my argument, otherwise I should not have a right to speak out, I realize that those who hold the ideas that I consider to be impossible are ready to turn the argument in their favor. I cannot help quoting here a beautiful and witty passage from *Through the Looking Glass*, which might be used by both sides in any disagreement on interpretation.

> "I can't believe that," said Alice. "Can't you?" the Queen said in a pitying tone. "Try again: draw a long breath, and shut your eyes."
>
> Alice laughed. "There's no use trying," she said, "one can't believe impossible things." "I dare say

* Presidential address to the 9th International Congress of Genetics, Bellaggio, Aug. 1953. Dedicated to his friend Otto Hahn on the occasion of his 75th birthday.

you haven't had much practice," said the Queen. "When I was your age I did it for half-an-hour a day. Why, sometimes I've believed as many as six impossible things before breakfast."

Now to the two philosophies of genetics to be contrasted. One is the statistical, or static, point of view; the other, the physiological, or dynamic, point of view. This antithesis does not mean that the two mental attitudes are mutually exclusive and could not be assumed simultaneously in their proper place. Nobody doubts that classical genetics is a statistical science and physiological genetics a dynamic one, each solving its own problems in its own way. What is meant is this. The statistical basic philosophy tries to interpret every generalized set of facts by the introduction of more and more units for statistical treatment. In the examples to be taken up subsequently, it will be seen that statistical thinking tries to explain all basic features of genetic phenomena by introducing more genes in the form of modifier systems built up by selection. In this way, a system is finally established, which is so conspicuous in much of present-day genetics, and which I must call hyperatomism and hyperselectionism. In my personal opinion, it will lead in the end to impossible consequences by requiring astronomical numbers of modifiers and a similar number of tiny but specific adaptations. This, I think, is an example of the "five or six impossible things" that the queen learned to believe before breakfast.

The physiological, or dynamic, approach, on the other hand, tries first to understand general phenomena in terms of genic action and developmental systems with all their consequences of interaction, embryonic regulation, and integration. Although this approach accepts, naturally, the basically statistical tenets of genetics, it tries, actually within the rule of parsimony, to avoid looking for explanations in terms of unproved, additional systems of units for more and more genic permutations. It prefers to find out how far explanations based upon the dynamics of the organism and its development under genic control will go. Let us illustrate the difference of mental attitude with a well-known example. In *Drosophila* populations, different inversions are found, differing in type and frequency in space and partly also in time. Without going into the details, this suggests that an adaptation brought about by selection is involved. Let us not discuss the merit of these facts but only the attitude toward their interpretation. The statistically minded investigator will look for systems of linked genes selected for a definite competition, which are protected from crossing over by the inversion and, thus, are kept in heterozygous condition. These blocks of genes are composed of such loci as are needed for adaptation to the particular environment. I am not discussing now whether this interpretation is correct but only the types of explanations for which different minds are looking. The geneticist who thinks in dynamic terms would look first for a possible function of the inversions. He would, for example, remember that inversions as such tend to change the time of development, and he would start experiments designed to find a physiological cause for the basic facts.

But let us get away from generalities and illustrate the alternative genetic philosophies with examples taken from the work of great geneticists whose philosophical outlook differs from mine. As the first example, I propose the theory of dosage compensation. The underlying facts are so clear that a detailed confrontation of the two basic types of interpretation is possible.

Sex-linked mutants in *Drosophila* are present in one dose in the male, in two doses in the female. Although normally this difference in dosage would lead to different quantitative expression of the trait, most sex-linked mutants appear identical in the two sexes. If the same mutations are made (by the use of duplications and deficiencies) to be present in one dose only in the female, they appear less extreme than in the male, and, vice versa, when put in two doses in the male, they are more highly expressed than in the female. This can be demonstrated, for example, for mutant eye colors and also for the normal type, which when checked photometrically shows the type of relationship just described. From these facts, the conclusion is drawn that the phenotypical identity of, in the present example, eye color in the two sexes is an adaptive trait and that this adaptation has come about by selection of dosage-compensating modifier systems for this sex-linked trait. The same reasoning will apply to all other X-chromosomal genes. All these modifiers must themselves be located within the X-chromosome, a conclusion that was first derived from dosage experiments with the bobbed alleles and later was studied in detail in eye colors. Thus the geneticist of statistical inclination turns first, if not exclusively, to an interpretation based upon extra genes and selection.

The geneticist of basically physiological persuasion would, from the beginning, look for an interpretation in terms of development. He would point out that male and female differentiation takes place in very different developmental systems laid down at the moment of fertilization by the different balance of the sex factors. He would point to the fact that developmental rates in the two sexes are different, that the relative rates for the individual and consecutive phases of growth are different, that times of determination as seen in temperature effective periods or in times for optimal production of phenocopies are different, and further, that the rhythm of differentiation of individual organs like the gonads differs in the two sexes. Thus, he would understand on the basis of different developmental systems why different dosages may fail to produce different phenotypes. He would also conclude that some developmental processes might be of such a kind that they would produce, in spite of the different development systems, different sexual phenotypes, as is known for a number of loci. This means that the loci in question act simply according to their dosage. The explanation that offers itself at once is that threshold phenomena are involved. The statistical geneticist would have to assume in this case that such sexually

dimorphic loci are of nonadaptational value and, therefore, are not in need of compensating modifier systems.

Let us go a little further into this interesting problem, not so much for the sake of proving that the dynamic type of explanation is the better one (although I cannot help but bring this out incidentally), but more with the intention of emphasizing further the contrast between the two basic ways of looking at genetical facts. The most recent student of the idea of dosage compensation does not fail to realize the possibility of an alternative interpretation. But he does not see this in terms of development—that is, genic action—but in terms of gene distribution. He says that the alternative is that the sex-determining genes themselves act as dosage modifiers. To disprove this, he points out some facts that are worth mentioning because they reveal so well the difference in basic outlook.

There is known a third chromosome recessive mutant, called "transformer," which in homozygous condition transforms 2X-females into what look to all purposes like males. If the eye color apricot is present, the transformed males have the same color as genuine males with apricot eyes. By introducing a duplication into a genuine male, it can be made to have two doses of apricot instead of one, with the result of a darker eye color. Therefore, the conclusion runs, the XX-males-by-transformation should have this darker color, if the sex determiners were also the dosage modifiers. Actually, the color is the same as in normal females and males, which means that not the sex determiners but the dosage compensators within the X-chromosomes are responsible.

This argumentation clearly assumes that the normal 1X-males and the transformed 2X-males are identical, which means that they have the same developmental system. If the problem had been looked at, not from the point of view of modifiers but from the point of view of development, it would have turned out that the males-by-transformation have a developmental system that is female in a number of basic features. Actually, the sex-reversal flies are not males but extreme female intersexes (=2X-intersexes) in which some basic features of growth and differentiation (actually those of early determination) are still female. This is true for size and general growth, for time of development, for many proportions, and for the rhythm of gonad development. In addition, all sex-linked mutants that are sexually dimorphic—that is, without so-called compensation—show the female phenotype. Thus, the behavior of the eye color is just what is expected in the 2X-intersexes and the dosage-compensation explanation becomes superfluous.

It is remarkable that similar ideas have also been used to interpret the fact that autosomal mutants frequently have a somewhat different expression in the two sexes; for example, they express themselves less intensively in the males. To mention only one example, mutants that produce extra veins on the wings of *Drosophila* have, as a rule, a less extreme expression on the male wing. If one studies the development of this character, one realizes that such differences may, in a general way, be dependent upon time relationships between the general speed of development of the wing and the special rates of concrescence of the wing membranes between the future veins. Although the details are not clear, the general idea is obvious to the geneticist who thinks in terms of development. A well-known population geneticist, who met with this fact of different sexual expression of such mutants found in natural populations, offered the following explanation, assuming *a priori* that the presence of such mutants in the population is an adaptive feature, based on correlated physiological properties.

> The different expression in males and females is probably also a reflection of the adaptive nature of this variation. The mutations . . . are pleiotropic, producing, on the one hand, extra veins on the wing, and, on the other, some physiological peculiarities which determine high viability. . . . Since in these populations free crossing occurs, it is apparent that the complexes of genes of extra venation must be the same in females and males. The question arises then, how is it that with an equality of the mutation complex in the two sexes, and with a different degree of sensitivity to them in males and females, there is in both sexes the same level of physiological adaptation? If a given complex of mutants is adapted for females, it should be harmful for males. If, on the other hand, a weaker complex is adaptive in males, it should be inadequate for females. Equality of the physiological manifestation of the same set of mutations in females and males can occur under these circumstances only in the presence of an additional regulating genotypic mechanism, which, for instance, may partly inhibit the action of these genes in males.

This then is a good example of the basic cleft between the two philosophies of genetics: One considers all and everything the product of selection and adaptation and, therefore, explains all observations by introducing specific modifier systems produced by selection, necessarily reaching, in the end, astronomical numbers. I cannot help feeling that the argument, as quoted, is queer, even perverted. The other philosophy looks for simple facts of development of the type just mentioned, which might automatically produce the effect without recourse to additional special and selective genic systems. In the special case under scrutiny, the geneticist who subscribes to this philosophy would add in support of his argument that the same sexual dimorphism in the phenotype of a mutant that led to the complicated assumptions reported is also present when the same mutant appears anew under his eyes, without any previous or following selection.

These examples lead to another group of facts which, for a long time, have demonstrated the same basic difference in genetic thinking—facts in the field of sex determination. If we confine our discussion to standard zoological bisexual material with genetic sex determination, such as *Lymantria*, *Drosophila*, and some fishes, we know that genetic sex determination is based upon the balance between female and male sex

determiners, the two possible normal balances being produced by the 1X-2X-chromosome mechanism, while imbalance produces intersexuality. One type of determiners is located in the X-chromosome and, therefore, is present in either one or two doses. The other type is located outside the X-chromosome, which means in different cases in the Y-chromosome, or in the autosomes or in both. Thus, one or two doses of one group of determiners are always opposed to the same dose of determiners of the other sex, independent of whether we are dealing with male or female heterogamety. In each case, the action of the determiners within two X-chromosomes wins over the action of the constant determiners of the other sex; while one X-chromosome, meaning the action of only one dose of X-chromosomal determiners, loses against the action of the determiners of the other sex outside the X-chromosomes. This then is the primary sex-determining mechanism. Derived from the analysis of intersexuality in *Lymantria,* it is based upon the relative dosage or balance of the sex determiners and is, thus, the starting point for all ideas on genic dosage and genic balance.

What does the mechanism control? It is at this point that the two different philosophies become patent. Sex determination by the balance system of sex determiners means first the control of production of the sex cells of one or the other sex, then of the gonads; of the accessory sex organs, such as ducts, glands, and genital armature; further, of all sexual differences in morphology, physiology, and behavior which—in *Drosophila* or *Lymantria,* for example—amount to differences in practically every organ and structure as well as in developmenal speed, rhythms, and many reactions. Maximally, every single cell of the body may be considered different in the two sexes.

The geneticist of statistical persuasion who wants to explain such profound differences is bound to look for a system of genes in which separable determiners for every differential trait are represented. Now, the facts of diploid intersexuality prove that any fertilized egg, be it a 1X- or a 2X-zygote, is able to develop into either sex or anything in between (that is, the series of male or female intersexes). In addition, every single one of the traits mentioned will be affected. Therefore, the statistical mind concludes that in the genome there always must be present all the innumerable genes that control the development of all the female, as well as of the male, traits. In the extreme case of all-pervading sex differences, this means the presence of two complete sets of all the genes concerned in the formation of the type of the species—that is, of practically all genes in strongly sex-dimorphic organisms.

The terminology for this type of genetic setup varies. Sometimes, this double group of genes is termed sex-promoter genes, sometimes one speaks of A and G genes or also of alpha and gamma. The balance mechanism then becomes a trigger or realisator mechanism, which takes care that one or the other set of sex-promoter genes is stimulated, or one or the other is suppressed, or both of these actions occur simultaneously. In detail, this may mean either that the balance between male and female trigger genes exercises this controlling influence, or that the trigger genes within the sex chromosomes effect this stimulation or suppression according to their dosage, without being sex determiners at all.

I consider the latter assumption incompatible with the experimental facts of intersexuality, but this point is not relevant for the present discussion. The decisive fact is that this point of view requires the assumption of special genes for every possible developmental feature in both sexes, with, in the end, two different complete sets for the sexual alternatives for each dimorphic trait, which may mean every single character of the species.

Let us now contrast with this picture the aspect of the problem as it is seen from the other basic point of view. Sex is a primary property of almost all organisms. Thus, the genetic determination of an organism contains also the possibility of a sexual alternative for, minimally, the sex cells and, maximally, for every cell of the body, with all gradations in between as seen in different organisms.

As a rule, the sexual alternative is decided by the genetic mechanism of sex determination. But the decision can also be brought about by external agencies. An injection of a genetically female chicken's egg with male hormone makes every cell, including the sex cells, decide for male differentiation. A female pupa of a gypsy moth will be induced to male development of the antenna by a temperature shock; a male pupa under the same conditions of experiment will start a female-like development of a part of the genital armature. Similar effects are produced by abnormal genetic constitution in the case of intersexuality. For example, one sex cell in an individual with one X-chromosome of proper genetic constitution will grow into an egg; another one nearby a little later, into sperm.

If we look for comparable cases outside the sphere of sex, we find cases such as these: The plant *Limnophila* produces normal leaves in air, laciniate leaves when grown under water. Many plants in juvenile condition have leaves that are completely different from those of the adult. Many fresh-water organisms, such as *Daphnids* or *Rotatoria,* assume largely different forms in warm or cold water. These and innumerable comparable cases are considered to be examples of the reaction norm concept of genic action. This means that genic action can be described only in terms of a specific external and internal (and also genetic) environment. In some cases, as in the plant *Limnophila,* this means an alternative norm of reaction, based upon, first, a genetic setup involving the possibility for an alternative norm of reaction and, second, an agency, here air and water, that decides the alternative.

Applying these models to the case of sex, we say that the genetic basis of sexual development is the ordinary one of the species. But some or all cells and organs have an alternative norm of reaction, male or female, also depending for decision upon an outside agency, the products of the sex determiners, which we

may call, in a general way, sex hormones without discussing the correctness of the nomenclature. Thus, we need no groups of female and male sex-promoting genes and the complicated process of selection that has built them up but only the unavoidable, general genetic constitution of the species, endowed with an alternative norm of reaction (which in detail is a problem of thresholds and probably an old, inherent property of sex, invented phylogenetically together with sex). With this genetic and physiological system, the products of the balanced sex determiners are reacting. There are many facts available to show that this simple system is present in well-studied material. But we do not want to go into the technicalities of the problem of sex determination. The point we want to make is only to show that the statistical attitude calls for explanations in terms of additional genes for whatever has to be explained, while the physiological attitude looks for interpretations in terms of genic action upon development.

There is, of course, no field of genetics in which the two basic attitudes are more pronounced than in the study of evolution. There is a reason for this. Selection is the uncontested major factor in evolution; and selection within varying populations, the prerequisite for evolution, is to a considerable extent a statistical problem. Thus, it is evident that the study of evolution via one of the approaches—namely, population genetics—is best suited to the statistical mind. This has led not only to very important insight but also, I may say even necessarily, to the extremest development of the statistical viewpoint as observed in the realm of Neo-Darwinian evolutionism.

It is primarily here that the way of thinking has developed which I called before hyperselectionism and hyperatomism. This means that innumerable individual groups of facts are explained as a result of selection involving more and more modifier systems, without inquiring whether this explanation is necessary. I do not mean by this the obvious phenomena of adaptation by selection of already present combinations of mutant loci, which are above discussion. I mean the trend to find selection behind almost any observed fact—for example dominance—or sexual differences of the type mentioned in the foregoing discussion of dosage compensation, or every instance of polymorphism, such as the ones mentioned before for wing-plexation and inversions in *Drosophila*. This attitude necessitates what I just called hyperatomism, the invention of more and more modifier systems upon which selection can work. If one were to put together all the cases for which such systems have been claimed, one would shudder at the number of otherwise unimportant genes needed to make the scheme work.

This viewpoint, powerfully aided by the fact that just such an imagined system lends itself to impressive mathematical treatment, neglects completely the fact that at the basis of all evolution is the organism itself. No evolutionary change is thinkable that is not contained within the developmental potencies of the organism; and, vice versa, any change of development—small, large, or very large—that is possible without major and unadjustable damage to the emerging individual may be the starting point for evolutionary diversification. Thus, the happenings within a varying interbreeding population studied from the point of view of selection of recombinations are only one aspect of evolution. The other aspect is the study of the potency for variation as seen in the potentialities of development, brought to light by proper experimentation. Again, I propose to take up a single example of an evolutionary problem and contrast the two ways of analyzing it.

The example is one that involves a major case of adaptation, quantitively far beyond the adaptations usually studied on the subspecific level, such as adaptation to climate, soil, and so forth—that is, all the types that I have called existential adaptations. I mean that part of the mimicry problem which deals with the mimetic polymorphism of butterflies. The well-known basic facts are these. In some species, a number of different types of females are found which look very different from the standard type of the species as preserved in the males or, sometimes, in one type of female. They resemble rather closely in form, pattern, and color poisonous members of different species, genera, or completely different families. In detail many different types are found: for example, only females are mimetic; both sexes are mimetic; only one mimetic type exists or a number of them; all females are mimetic; mimetics and nonmimetics are present among females.

We shall consider only one case, in which all females are mimetic and are of two or three widely different phenotypes, mimicking poisonous members of other families. We may accept it as a fact without further discussion that this is a case of true mimicry protecting the mimics from their enemies. The decisive fact that makes this case a good example of the alternative philosophies of genetics is that, in all cases in which the genetics is known, the mimetic types differ from one another and from the nonmimetic type by simple Mendelian differences involving one or two pairs of alleles, the recombinations of which produce all the known types. The discoverers of these facts drew the obvious conclusion that such huge evolutionary departures as are involved here can be produced in a single step by simple Mendelian mutation. The chief proponent of the Neo-Darwinian type of selectionism realized, however, that here was a test case for his views and, therefore, developed an interpretation in conformity with the statistical philosophy. He starts, as is well known, from the idea that selection acts upon the gene complex, not upon the individual locus modifying the response of the organism to the particular single locus in question, which itself remains unchanged. The classic application of this idea is found in the theory of the origin of dominance by selection of modifiers. The decisive point for the present discussion is that the basic activity of a gene may be completely unaltered while selection acts upon modifiers for the phenotypic end-effect. In polymorphic forms,

this selection will be more rapid, because the heterozygotes will be more plentiful. When now a mutation produces by chance a "remote" resemblance to a more protected species, from which "some advantage, however small," may be derived, the deception will constantly be improved by selection of the proper modifier system. This, working in the end upon the whole residual heredity, will result in a gradual change in the effects of the gene concerned. But the gene itself is unaltered and remains as a switch, turning on one or another set of characters, subject to variability and selection.

We do not intend to discuss the facts considered to favor this ingenious interpretation or the criticism that can be leveled against the entire group of interpretations when the facts are analyzed in detail. We just state that here is a typical example of the statistical philosophy of genetics and contrast it with the way the opposite type of mind would look at the facts. In view of the basic fact that genetic differences between the mimetic and the nonmimetic and among the different mimetic types appear to be simple Mendelian differences, the geneticist who thinks dynamically in terms of genic actions would ask himself first whether it is possible, on the basis of known facts of development and phenogenetics, that the huge differences in form, color, and pattern between these forms can all be based upon simple chance mutations which at once offer to selection the complete, or almost complete, array of adaptive traits. He would, therefore, enter into the details of pattern formation on the Lepidopteran wing. He would find that mutants exist which affect only small features of localized parts of the pattern, including color; that other mutants affect simultaneously a series of such features; and that still others affect basic features of the patterning process, such as presence or absence of bands, or their typical localization. In conformity with other knowledge, he would conclude that the earlier the genic action upon the processes of pattern determination takes place, the more extensive the change will be. He would then inquire into the potentialities of the developing wing for change in pattern without genetic change. There he would find, among many important facts, the cases of seasonal dimorphism in which the same species can develop two different patterns, sometimes as different as, or even more different than, the mimetic patterns under discussion, and controlled in nature and experiment by temperatures and by the hormones for the initiation of diapause. He would also find instances in which extreme sexual differences, of the order of magnitude of very large mutations, can be completely equalized by simple experimentation, for example, the use of temperature shocks. He would also remember that all known mutants of *Drosophila*, small or large, can be mimicked phenotypically in the experiments on phenocopy, with the corollary that the ability of the organism to undergo large genetic changes in a single step is limited only by the power of the developing organism to change development considerably and, nevertheless, produce a harmonic whole by embryonic regulation and integration. Thinking analytically in such directions, he would come to the conclusion that the production of the mimetic patterns as single mutant steps is within the domain of the potentialities of development and, therefore, he would feel no need for switch genes and selected modifiers and would look critically into any and all alleged proofs for their existence.

Only one more example for the two opposed philosophies will be presented, one which I believe to be pregnant with future possibilities for the understanding of the ultimate problems of genetics. During the past 15 years ideas on the nature of the genetic material in the chromosomes have been developed, which are rather different from those of classic genetics and, therefore, were not too well received in the beginning but now are attracting an increasing number of friends. Confining the discussion to the topic of the present address, these ideas try to replace the statistical, atomistic views of classic genetics by a dynamic, relational view which sees in the chromosome a heirarchical system of a polarized structure, the parts of which may function in different subunits of hierarchical order. We chose from the groups of facts from which such views were derived only one, which permits again the contrasting of the two genetic philosophies and points to the one which offers hope of future biochemical analysis.

A long time ago, it was realized that the phenomenon of multiple allelism was best suited for attacking the problem of the nature of the gene and its action. A first step beyond the classical concept of the gene was made when multiple alleles were conceived as different quantities of genic substance, thus introducing the dosage concept into the gene itself. A step still farther away from the classic gene was made when a group of Russian geneticists introduced the idea of step-allelomorphism, which claimed, within a group of multiple alleles, a definite and strange spatial arrangement within the chromosomal segment called a gene. Although both these ideas were unable to survive in their original form, their basic attitude pointed in the right direction.

It has since become clear that in *Drosophila* the genetic loci in the chromosomes are segments of different lengths, some containing up to an unknown maximum number of salivary gland bands, these segments constituting physiological units. This means that whatever happens within such a segment produces a definite effect—namely, that of a mutant—with small variations according to the individual causative happenings. To take a concrete example: within a group of bands in the scute or yellow regions so-called point mutation can occur—that is, a mutative change which cannot be detected with the light microscope. The effect will be a scute or yellow phenotype, respectively. If within the same region and at any interval a rearrangement break occurs, the scute (or yellow) type again appears as a position effect. All these changes of whatever kind not only produce the scute phenotype with typical small differences but also con-

stitute a group of multiple alleles. Allelism is, thus, bound to the section in question and applies to whatever change occurs within the segment.

Let us first look at the explanation that such facts have received on the basis of the classical theory, which means, for the present discussion, derived from the statistical philosophy. This explanation is based upon one partial fact not yet mentioned, namely, that crossover breaks can occur within such a segment with the result that what were considered before two or three alleles now become separable genetic units and are, therefore, called different genes. But in spite of this the two actions remain allelic. This means that, if each of a pair of chromosomes contains at least one of the recessive mutant loci, we get the homozygous phenotype. In order to explain this basic fact, it is assumed that the two or three and in some cases many loci that can be separated by crossover breaks are duplications, triplications, and so on, of one original gene. After duplication, the new gene assumed a somewhat different function of the type of a multiple-allelic difference. But its faculty of being allelic remained, but only if the old and the duplicated genes are located in different homologous chromosomes. Therefore, the phenomenon is called pseudo-allelism and the alleles, position alleles. A corollary of this is that the duplicated genes might, in time, become so different that they no longer affect the same character and lose their allelism.

The alternative explanation is based on the recognition of the segments of identical action already mentioned and the fact that submicroscopic mutation, as well as position effect within the segment, produces multiple alleles. Thus, it is the normal or disturbed order, visible or invisible, that distinguishes the normal and the mutant effect. Since the segment is the unit of action, controlling, say scute or yellow if changed, changes in homologous chromosomes are allelic, and there is no need for pseudo-allelism and position alleles. The reason for this is obviously that the whole segment is in control of one chain of reactions which will be interfered with in a similar way by whatever change happens within the segment, producing always, for example, a scute or yellow effect. But here a quantitative element enters: if the segment is taken apart by a rearrangement break or organized in a different order after a crossover break, the chain of reactions still of the same type—for example, leading to yellow pigment—is affected quantitatively to produce the slightly different phenotypes of the yellow alleles. Thus, by the way, crossing over, a purely mechanical feature happening wherever the breakable parts of the chromosome are found, does not enter the definition of the basic unit. It may also happen within it.

The great difference between the two interpretations of the same facts is that the statistical one leaves room only for more and more genes of the same type and has to invent specific features, such as position alleles, to explain facts beyond the scope of the classic gene. The dynamic interpretation not only unifies the different facts as the product of one single structural principle. In addition, it leaves room for future developments that might lead to real biochemical understanding. If sections of basic action are integrated into the next higher hierarchical unit, one can conceive —forgetting completely the gene—that they control, again as a unit, nearly related but branching chains of reactions, which control larger elements of the developmental process. I would look for such an explanation if it is found that mutants affecting the same organ are frequently located within a larger section of the same chromosome. In the same way, a hierarchy of action could be conceived, up to the chromosome as a unit of action. It is improbable that, in a higher organism, the biochemical meaning of such a hierarchy could be elucidated, except in the cases where serological effects are involved. But in microorganisms, facts have already been found that give some hope that here further insight is possible. My own personal opinion is that the classic theory of the gene will lead only into a blind alley in this search for the biochemical nature of the hereditary material, while the way of thinking which I called the dynamic philosophy of genetics will lead to ultimate success.

Apart from purely genetical considerations, there is also a very general reason for the attitude I have taken. This is the fact that the hierarchical order is clearly essential in living nature, although it also exists in inanimate nature, as the order nucleus and electron, atom, radical, molecule, macromolecule, crystal shows, each higher member of the hierarchy being composed of the lower ones but different in its qualities from a mere sum of these. It is clearly not the sum but the orderly relationships of the components that are responsible for the actions at the different levels of the hierarchy. Therefore, at these different levels also, new types of interrelationships appear, say in inorganic nature the Van der Waals forces on top of ordinary valencies. In view of such facts a biologist, studying a clearly hierarchical system of activities like that of chromomere, chromosomal segment, chromosome, genome, would hardly expect to meet with a situation even simpler than that present in inorganic nature—namely, total action being the sum of all partial actions, as assumed in the classic theory of the gene. He would rather expect to find a still more complicated relationship in which the parts, in a hierarchical order work together via spatial relationships, orders, patterns. This is one of the reasons why I am convinced that the new way of looking at the nature of the genetic material will have to supplant the statistical classical theory of the gene, before the attack on the ultimate biochemical problems is possible. But with these statements I have already gone beyond the scope of contrasting what I consider to be the two basic philosophies of our great science and fallen into the trap of stating my own opinions.

The four examples that I used to contrast the two major philosophies of genetics were, I think, a fair sample of basically different interpretations of facts. I did not try to hide, and as a matter of fact would

not have succeeded if I had tried to hide, on which side my own sympathies are found. This does not mean that I am blind toward the merits or ungrateful for the brilliant results of the work of those whose basic philosophy I do not share. I am perfectly aware of the fact that science, in all its different fields, makes progress only by the clash of ideas, which are not all good or all bad, but good only as far as they give inspiration to new experimental attacks. What becomes, in the end, of either of the opposing ideas is rather unimportant. Probably neither of them will survive finally. But while we are working and trying to open new ways of attack on basic problems, it will be helpful to stop occasionally, look at the basic philosophies lying behind our mental procedure when deriving generalizations, and in doing so clarify our own thoughts by analyzing different thoughts sympathetically but also critically. Then it will turn out, after all, that the Queen in the storybook acted under some illusion when she practiced believing a series of impossible things before breakfast—namely, the illusion that anybody could decide what is possible or impossible. But there is at least one thing we can do, which Willard Gibbs expressed in these words: "One of the principal objects of theoretical research in any department of knowledge is to find the point of view from which the subject appears in its greatest simplicity." Convinced of the correctness of this statement by a great thinker, I have repeatedly prefaced works of mine with the old formulation of the rule of parsimony *"Frustra fit per plura quod fieri potest per pauciora."* This is exactly what I have tried to apply also today. If I have failed I must exclaim with Job: "Is there iniquity in my tongue? Cannot my taste discern perverse things? Teach me, and I will hold my tongue: and cause me to understand where I have erred."

Some Aspects of the Chemistry and Biochemistry of Cholesterol*

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CHOLESTEROL, discovered by Chevreul in 1815 and readily available for experimentation from gallstones or brain, has been the subject of innumerable researches for more than a century, but it still presents certain problems of interest that are under active inquiry. This solid alcohol of the formula $C_{27}H_{45}OH$ is no minor constituent of the animal body. The total quantity of cholesterol in a man weighing 65 kg is approximately 210 g, or 0.3 percent of the wet weight (*1*). The largest amounts are present in the skin (51 g) and nervous tissue (35 g); the tissue concentration varies from 0.14 percent (muscle) to 4.5 percent (adrenal gland). The sterol normally present in plasma to the extent of 0.2 percent is partly free (27 percent) and partly as esters of higher fatty acids, while that present in red blood cells (0.12 percent) and in nervous tissue (1.9 percent) is completely unesterified. The cholesterol of herbivorous animals is derived exclusively by biosynthesis, while that of man is supplied by a combination of biosynthesis and diet. R. P. Cook has demonstrated (*2*) that the intake of 0.58 g of cholesterol per day from an average normal diet (*3*) can be increased to 6.9 g by a regime of menus involving consumption of 20 eggs per day.

What is the role of cholesterol? In what way or ways is it useful to the animal organism? The free cholesterol of nervous tissue appears to serve the function of forming a component of a structural unit of the tissue; Finnean (*4*) has postulated a specific orientation of the molecules of cholesterol and phospholipid in a complex that, in combination with protein, constitutes the structure of myelin. It seems to me likely that the cholesterol in plasma plays a key role in the transport of neutral fat, by the mechanism suggested in the following idealized representation:

$$\text{Lipoprotein A}\begin{cases}\text{protein}\\ \text{phospholipid}\\ \text{cholesterol}\\ \text{glycerides}\end{cases}\underset{+\text{ glycerides}}{\overset{-\text{ glycerides}}{\rightleftharpoons}}\text{lipoprotein B}\begin{cases}\text{protein}\\ \text{phospholipid}\\ \text{cholesterol}\end{cases}$$

The protein may be the cart, and the lipid part of the sterol may supply a lining for reception of the cargo of other lipid. A possible function of the free cholesterol present in high concentration in the membrane of the red blood cell is to form complexes with, and so detoxify, substances that otherwise would have a hemolytic action (*5*). The metabolism of cholesterol is surely associated with that of the steroid sex hormones and cortical hormones, since Bloch (*6*) has demon-

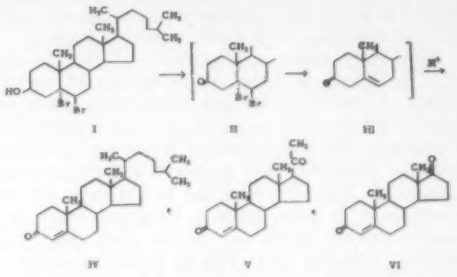
* A lecture delivered in Paris, Nov. 13, 1953, under the auspices of the Société Chimique de France and the Société de Chimie Biologique.

strated conversion of cholesterol into pregnanediol, a metabolite or progesterone. It is possible that cholesterol serves as precursor both of these hormones and of vitamin D_3.

Is cholesterol, on occasion, also involved in pathological changes? It is assuredly involved in the formation of gallstones, since these are composed of free cholesterol to the extent of 70 to 80 percent, and in hypercholesteremia, which may be attended with a three- or fourfold increase in blood level. It is involved also in arteriosclerosis, since the sterol content of arteriosclerotic aorta is 5 to 50 times that of normal aorta, but the question of whether or not cholesterol is a causative agent is still uncertain. Myxedema, a disease due to hypofunction of the thyroid gland, is characterized by lowered rate of basal metabolism and augmentation in blood cholesterol. There are some suggestions of an involvement of a spleen sterol in thrombocytopenic purpura (*7*) but the evidence is very tenuous.

The problem that I wish to discuss in particular is that of the possible carcinogenicity of cholesterol, or of some related or derived substance. I became interested in the problem as the result of a conversation in London in June 1950, with Sir Ernest L. Kennaway, who, while on retirement from his post as physiologist at the Chester Beatty Research Institute of the Royal Cancer Hospital, had followed with growing interest the results of a study conducted by his associate, I. Hieger. Hieger had observed (*8*) that subcutaneous injection of cholesterol in lard solution into several hundred mice resulted in 4 to 6 percent incidence of slowly developing (18 mo) tumors at the site of injection. It seemed to me that cholesterol itself, which is so widely distributed in the body, could hardly have the properties of a carcinogen of even low-order potency but that the tumors appearing at the site of the injected material must have been initiated by some transformation product of cholesterol or some unknown companion substance.

I then recalled the extraordinary observation of Bischoff and Rupp (*9*) that injection into mice of a crude commercial progesterone preparation afforded slowly developing tumors in 32 percent of the animals tested, whereas pure progesterone proved to be wholly noncarcinogenic. The crude progesterone preparation was obtained by a method developed by Spielman and Meyer (*10*) that consisted in oxidizing cholesterol dibromide with acidic permanganate in a benzene-water system, followed by debromination with zinc and acetic acid, a process attended with migration of the double bond from the Δ^5-position (III) to the Δ^4-position (IV, V, VI). Extraction of a petroleum ether solution of the reaction mixture from 50 g of cholesterol with concentrated hydrochloric acid removed an oil containing, according to bioassay, 100 mg of progesterone (V). A small amount of androstenedione (VI) was also isolated from this oil, which is the material Bischoff and Rupp had found to be carcinogenic. From the residual material not extracted by acid, Δ^4-cholestene-3-one (IV) was isolated in over 50 percent yield. Pure samples of the two known by-products, IV and VI proved, like progesterone, to be noncarcinogenic.



The two series of experiments seemed to me to suggest the existence of a nonaromatic, possibly endogenous, steroid carcinogen related to cholesterol. The discovery that the polycyclic aromatic hydrocarbon methylcholanthrene is a highly potent carcinogen (*11*) and that it can be produced in the laboratory, albeit by pyrolytic reactions, from normal constituents of the body—namely, desoxycholoric acid (*12*), cholic acid (*13*), and cholesterol (*14*)—suggested the hypothesis that cancer may originate through abnormal metabolism of a sterol or bile acid to an aromatic hydrocarbon such as methylcholanthrene. The estrogenic hormones are probably correctly described as partially aromatized sterol derivatives: estrone, estradiol, and estriol contain one aromatic ring; equilenin contains two. Methylcholanthrene contains four aromatic rings, and a reasonable if wholly speculative pathway for its metabolic formation from adrenal cortical hormones has been suggested (*15*). However, all attempts to demonstrate the *in vivo* conversion of a natural steroid to an aromatic hydrocarbon of the type of methylcholanthrene have failed, and the accumulated evidence of 19 yr of research on the subject strongly discounts the possibility that such a process can be a cause of cancer. However, there is nothing to exclude the possibility that some transformation product of a natural steroid other than an aromatic hydrocarbon is capable of initiating malignant growth. The property of carcinogenicity is now known not to be specific to hydrocarbons of the methylcholanthrene and benzpyrene type but to be exhibited, in varying degree and kind, by such structurally distinct compounds as *o*-aminoazotoluene (*16*), 2-acetylaminofluorene (*17*), and vinylcyclohexene diepoxide (*18*). Carcinogens of still other types may well be possible, including the steroid type that I have postulated. The cholesterol examined by Hieger and the crude progesterone examined by Bischoff and Rupp might conceivably contain some elaborate substance roughly related to vinylcyclohexene diepoxide, but it could hardly contain any nitrogen compounds or any aromatic hydrocarbons. All previous attempts to demonstrate the *in vivo* formation of a carcinogen from a steroid or to detect such a substance in cholesterol, as such or after

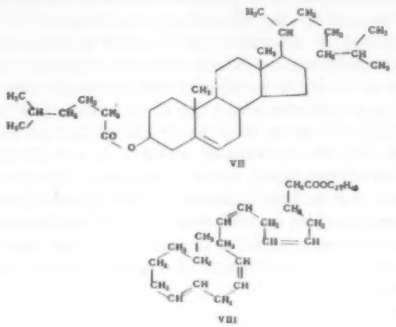
heat treatment or irradiation, have been based on the assumption that the carcinogen is aromatic and have involved searching for something having the spectrographic characteristics of an aromatic compound. I decided to search for a substance still having the chemical characteristics of a sterol or steroid hormone.

My inquiry, begun in the summer of 1950, has led to a succession of alternate hypotheses of varying degree of attractiveness and plausibility. Each has pointed the finger of suspicion at some compound or compounds that have appeared worthy of investigation, and these have been prepared in pure form and supplied to laboratories willing to test them for carcinogenicity in mice. Such a biological assay is a lengthy process. In the two studies cited, the tumors observed appeared only after an induction period of about 18 mo. A compound cannot be declared to be negative until all the mice have died, after perhaps 28 mo, and even then one can say only that the compound is negative under the particular conditions selected. Hence, definitive reports from the cooperating biological laboratories are not yet available for evaluation of any of the hypotheses to be presented.

The first idea was suggested to me by the fact that, in their control experiments, Bischoff and Rupp observed no tumor production from cholesterol injected into mice in sesame oil or in colloidal aqueous dispersion, whereas the tumors observed by Hieger resulted from injection of cholesterol in 20 percent solution in lard. The long period of incubation of the implanted cholesterol-lard mixture could afford opportunity for a transesterification that might produce an ester of cholesterol with a fatty acid abnormal to the particular tissues of the injection site. Differences have been noted in the amounts of ester cholesterol and phospholipid in the cell nuclei of normal and tumorous rat livers (*19*), and Leary (*20*) has expressed the view that crystalline ester cholesterol deposited focally is the stimulating agent responsible for the growth of benign cortical adenomas in man.

That the Spielman-Meyer process affords both cholestenone and progesterone shows that the side chain is in part retained and in part subjected to oxidative fission. Since methyl isohexyl ketone is a known product of oxidative fission of the side chain (*21*), isoheptylic acid might have been produced in the oxidation step; the final partition of the reaction mixture between petroleum ether and concentrated hydrochloric acid could have effected esterification of unchanged cholesterol with such an acid. As far as is known, cholesteryl isoheptylate would be abnormal to subcutaneous tissue in respect both to the odd-carbon content and the branching of the fatty acid component (*22*).

Hence, cholesteryl isoheptylate (VII) was synthesized (*23*) and submitted for assay, along with a few other esters, including the arachidonate (VIII). Arachidonic acid seemed of interest as an acid component, since this tetraunsaturated C_{20}-acid is present in the fatty acids of human depot fat to the extent of only 0.6 percent (*24*) but accounts for 22 percent of the fatty acids of the phosphatid fraction of beef adrenal glands (*25*). Also, when the formula is arranged as in VIII, the multiple double bonds would seem to afford invitation for cyclization to a steroid-like structure.



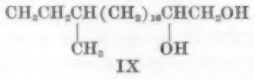
VII

VIII

A second, rather vague idea, was that the suspected steroid carcinogen might be a hitherto unknown or unexplored product of oxidation of cholesterol, possibly a variant of one of the hormone structures. In the search for some unusual oxidation product, I reinvestigated extensively both the partial (*26*) and exhaustive (*27*) oxidation of cholesterol with hexavalent chromium derivatives. The structures of two of the five known oxidation products were elucidated, and three new products were isolated. The main pathway of oxidation was shown to proceed through initial dehydrogenation of cholesterol to Δ^5-cholestene-3-one, represented in the foregoing formulas as the hypothetical intermediate III. A very remarkable product of partial "oxidation" was identified as epicholesterol, a product of rearrangement regarded as resulting from a process of addition-elimination of chromic acid to the double bond. The third new product is a still unidentified substance of the formula $C_{27}H_{44}O_3$ temporarily designated Ketone 104 (*28*), since the first isolation was recorded on page 104 of my notebook (Vol. 23). The substance, formed in only 1 percent yield, was at first (*28*) thought to be derived from a companion substance but has been shown since to be derived from pure cholesterol. It is surely of an unusual structural type, as can be seen from a tentative formulation presented later in this discussion, and it is under assay for carcinogenicity, although there is no reason to suspect that it has any physiological activity or can arise in the body.

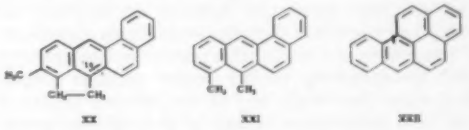
My oxidation experiments had afforded extremely small amounts of other products that I thought could not have come from cholesterol itself, and I was thus led to reinvestigate the question of the homogeneity of sterol extractable from animal tissues. Windaus and Stange (*29*) had isolated the companion 7-dehydrocholesterol (provitamin D_3) by chromatographic fractionation of 2 kg of egg yolk cholesterol containing 0.18 percent of provitamin by spectrophotometric analysis in a series of elutions utilizing more than 1000

liters of solvent. Schoenheimer (*30*) had presented indirect evidence suggesting the presence in cholesterol of the reduction product cholestanol. I established the presence of cholestanol unambiguously by direct isolation (*28*) and isolated as well an isomer of cholesterol characterized as Δ^7-cholestenol (*28*); for material of biological origin, I have suggested the name lathosterol. My coworker, Bidyut K. Bhattacharyya, isolated the further companion cholestane-3β, 5α, 6β-triol (*31*), and the Italian workers Ercoli and de Ruggieri (*32*) have isolated a component designated cerebrosterol and characterized as 24-hydroxycholesterol. In work yet not reported, I have confirmed their isolation of cerebrosterol and have isolated from wool fat (degras) a further substance that my assistant, Wei-Yuan Huang, has characterized as not a sterol but a diol of the probable formula IX. It is related to batyl, chimyl, and selacyl alcohol, which are ethers of the type $ROCH_2CH(OH)CH_2OH$ (*33*).



IX

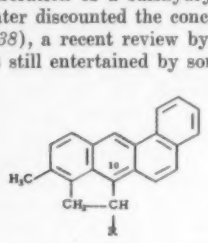
Lathosterol is a regular constituent of tissue sterol, and the amount present is so great (0.5–3 percent) that the substance can hardly be a carcinogen *per se*. It is much more sensitive to oxidation than cholesterol, and hence oxidation under a variety of conditions was investigated to see whether any of the products might have potentialities as possible carcinogens. One striking and unique characteristic of the Δ^7-stenol is that, on oxidation as free alcohol or acetate with hexavalent chromium or with peracids, it affords ketoxides (XI, XIII, XIV) or oxido alcohols (XV, XVI), which bear some resemblance to the carcinogenic epoxides described by Hendry *et al.* (*18*). Study of the reaction with selenium dioxide in acetic acid (*34*), which proceeds with bond migration to give XVII, was of particular importance in establishment of the configurations of the aforementioned epoxides. Oxidation under very mild conditions with mercuric acetate, bromine, or N-bromosuccinimide effects dehydrogenation to the 7,8,9,11-diene XVIII, which is a type recently studied intensively as a key intermediate for the synthetic production of cortisone from natural sterols. Thus, oxidation of XVIII with a variety of reagents results in introduction of oxygen at C_{11} either as a keto group (XIX) or as an epoxide. The two steps of oxidation proceed so easily as to suggest that the lathosterol present in lard-injected cholesterol may be oxidized by peroxides present in the lard to an 11-oxygenated steroid that might contain one or two epoxide groups. The possible carcinogenicity of such products is under investigation. Since the first step in the Spielman-Meyer process is a bromination, the lathosterol present could have been dehydrogenated to a diene of type XVIII, and the carcinogen could be a product of oxidation of this substance.



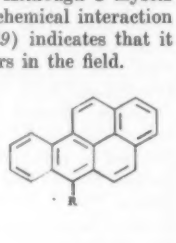
XX XXI XXII

Still another hypothesis, the most recent one, resulted from an entirely different line of reasoning. In the period 1935–43, my research group studied extensively the correlation of carcinogenic activity of aromatic hydrocarbons with structure and with chemical reactivity. By, so to speak, dissecting the methylcholanthrene molecule (XX), we were able to show that some structural features are unimportant, while others make major contributions to carcinogenic potency. Thus, the methyl group can be left off and the five-membered ring opened without loss in activity, since XXI is a potent carcinogen. It is particularly important that the molecule contain a 1,2-benzanthracene ring system with a carbon substituent at the meso position 10. 3,4-benzpyrene (XXII), a second highly potent carcinogen, also has the 1,2-benzanthracene ring system and this possesses a carbon substituent at the meso position 9. We then found that these two potent carcinogens are endowed with remarkable susceptibility to substitutions, manifested in the unique reaction of diazo coupling (*35*), in oxidation by lead tetraacetate at a low temperature (*36*), and in condensation with thiocyanogen (*37*). Under comparable conditions, ordinary aromatic hydrocarbons and less potent carcinogens are inert, and a definite if rough correlation seems to exist between carcinogenic potency and chemical reactivity. Furthermore, the point of attack in the substitutions of methylcholanthrene is at the methylene group at the meso position 10 (XXIII), a center deduced in the other study to be of particular importance to carcinogenic potency. In 3,4-benzpyrene the point of attack is at a position cor-

responding to C_{10} in the 1,2-benzanthracene ring system. In 1941 (*15*), I suggested that production of tumors in animals after injection of these hydrocarbons may be dependent on their special chemical reactivity and may be initiated by interaction of the hydrocarbon with the disulfide link of a proteinoid enzyme, with attachment of the hydrocarbon and liberation of a sulfhydryl group. Although I myself later discounted the concept of a chemical interaction (*38*), a recent review by Wolf (*39*) indicates that it is still entertained by some workers in the field.



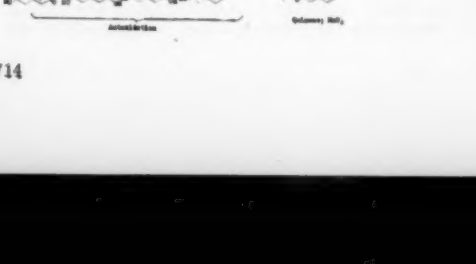
XXIII



XXIV

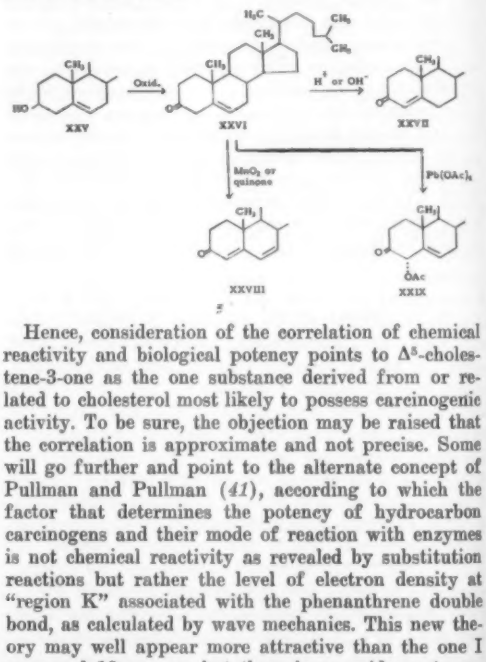
(R = -N=NC$_6$H$_4$NO$_2$, -OCOCH$_3$, -SCN)

Irrespective of the question of the mode of action, the empirical correlation between carcinogenic potency and chemical reactivity seems highly significant. Furthermore, it is remarkable that methylcholanthrene and 3,4-benzpyrene exhibit similar chemical properties, since they really are of two distinct types; in the first, substitution occurs in a methylene group, whereas in the second it occurs in an aromatic ring. It would seem possible that a substance of still a third type having comparable chemical reactivity might exhibit comparable biological actions. Does any companion of cholesterol, or any product of oxidation of the sterol or its companions, possess the distinctive chemical reactivity of methylcholanthrene and 3,4-benzpyrene? Not, I think, any of the known companions or any of ther oxidation products discussed in foregoing paragraphs. The pattern of chemical oxidation of cholesterol itself is extremely complex, since no less than 21 oxidation products are now known having the intact C_{27}-skeleton and resulting from direct oxidation without protection of the double bond. These are indicated in the chart, "Products of oxidation of cholesterol." Attack by dichromate is particularly diversified, since it affords eight products; the last formula in the top line is that tentatively assigned



to Ketone 104. The substances formed by oxidation with other reagents are all well-known products, except 25-hydroxycholesterol, listed as a product of autoxidation. I have found this substance present in commercial cholesterol that had been stored for 4 to 24 yr but not in material freshly manufactured by the same process.

Among these many substances derived from cholesterol by oxidation, there is just one that meets the specifications outlined, namely, Δ^5-cholestene-3-one (XXVI). The methylene group at C_4 is activated by the carbonyl group on one side and the double bond on the other, and it does indeed have the same high degree of sensitivity to substitution as the meso-methylene group of methylcholanthrene and the meso nuclear position of 3,4-benzpyrene. Thus Δ^5-cholestene-3-one is oxidized by lead tetraacetate at 15°C to the 4α-acetoxy derivative XXIX (*40*). It also couples with *p*-nitrobenzenediazonium chloride and absorbs molecular oxygen in boiling benzene, but the products have not yet been characterized. Δ^4-Cholestene-3-one (XXVII), to which the Δ^5-ketone is easily isomerized by acid or base, does not share this reactivity, nor does cholesterol or any of the other products of its oxidation.



XXV XXVI XXVII XXVIII XXIX

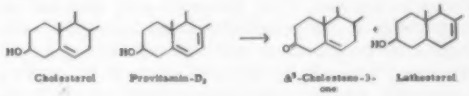
Hence, consideration of the correlation of chemical reactivity and biological potency points to Δ^5-cholestene-3-one as the one substance derived from or related to cholesterol most likely to possess carcinogenic activity. To be sure, the objection may be raised that the correlation is approximate and not precise. Some will go further and point to the alternate concept of Pullman and Pullman (*41*), according to which the factor that determines the potency of hydrocarbon carcinogens and their mode of reaction with enzymes is not chemical reactivity as revealed by substitution reactions but rather the level of electron density at "region K" associated with the phenanthrene double bond, as calculated by wave mechanics. This new theory may well appear more attractive than the one I proposed 12 yr ago, but there is no evidence to exclude the older theory, and in any case it has suggested the experiment of testing Δ^5-cholestene-3-one for carcinogenicity. A negative outcome of the test would not spell a complete victory for the theory of Pullman and Pullman over mine, for any theory must admit of an exception in which some accessory property is

lacking, such as appropriate solubility, absorbability, molecular dimensions, chemical stability, or resistance to metabolic destruction. The theory of Pullman and Pullman is based on a theoretical analysis of aromatic systems and, hence, would not predicate carcinogenicity in Δ^5-cholestene-3-one or any other nonaromatic steroid, but the evidence that such a substance has indeed been responsible for tumors evoked in mice by preparations from cholesterol has seemed to me more convincing than the theoretical argument to the contrary.

Of the various candidate steroids postulated as possible carcinogens Δ^5-cholestene-3-one seems to me the most promising (*42*). It is only 2 hydrogen atoms removed from cholesterol and is the initial product of oxidation with hexavalent chromium, of dehydrogenation with copper oxide, of oxidation with manganese dioxide or by the Oppenauer method. That it has never been isolated from animal tissue is of no great significance, since it is a very labile and reactive substance that one could hope to isolate only by a very special process or as some characteristic transformation product. Saponification or treatment with acids isomerizes the substance to the conjugated ketone XXVII, and such mild agents as manganese dioxide and quinone (in the presence of aluminum alkoxide) oxidize it to $\Delta^{4,6}$-cholestadiene-3-one (XXVIII). Thus, the Δ^4-cholestene-3-one isolated from swine testes (*43*) and the $\Delta^{4,6}$-cholestadiene-3-one isolated from swine spleen (*44*) and from arteriosclerotic aorta (*44*) may have been derived from Δ^5-cholestene-3-one initially present. Lederer *et al.* (*45*) isolated coprostanone from ambergris and inferred that it is a precursor of coprostanol and epicoprostanol, which had been isolated earlier from this source, and that it must have been derived from Δ^5-cholestene-3-one, formed initially by oxidation of cholesterol.

The hypothesis regarding Δ^5-cholestene-3-one does not help much in clearing up the mystery of the carcinogenicity of the Spielman-Meyer progesterone. The crude reaction mixture formed in the debromination step may well have contained considerable Δ^5-ketone as the result of incomplete isomerization, but this probably would have been isomerized fully in the subsequent treatment with hydrochloric acid and surely would not have been extracted by the acid in unaltered form.

Early claims purporting to show that cholesterol acquires carcinogenicity on irradiation with ultraviolet light or on heat treatment (*46*) take on a somewhat different aspect when considered in the light of the present speculations. Thus A. H. Roffo's extensive work on the feeding of irradiated cholesterol to mice (600 test animals, 1000 controls) has been largely discounted, because his claim to have identified polycyclic aromatic hydrocarbons from the irradiated material could not be substantiated by others; but if the carcinogen thought to result from photoxidation were a steroid, it might well have escaped detection, particularly if it were the labile Δ^5-cholestene-3-one. This ketone conceivably can arise by a process other than oxidation—namely, by disproportionation, a reaction often induced by heating. The hydrogen acceptor could be cholesterol itself, which would afford the known companion cholestanol. However, the 5,6-double bond of provitamin-D_3 is more reactive (hydrogenable with Raney nickel) than that of cholesterol and, hence, a more likely process of disproportionation is that formulated:



The three alcoholic components are all normal constituents of tissue sterol, which would make the fact of hydrogen exchange all the more likely to be overlooked.

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News and Notes

125th National Meeting of the American Chemical Society

An appeal to America's scientists to strive for greater public understanding of—and support for—free, uncommitted research was made by Louis P. Hammett, head of the Columbia University chemistry department, in an address at the American Chemical Society's 125th national meeting, held in Kansas City, Mar. 23–Apr. 1. The address, marking Columbia's bicentennial, was presented at a general session of the Society. Discussing "Rights and responsibilities in the search for knowledge," Prof. Hammett linked the nation's prospects for survival to the new weapons and other discoveries that may be expected from unprogrammed research in view of the great contributions made by such research in the past. There is no reason to suppose, Prof. Hammett said, that we can keep ahead of our potential enemies indefinitely with respect to programmed and outright developmental research, "particularly if they continue to produce technically trained men faster than we do." He pointed out that the Communist philosophy scornfully rejects exploratory research that has no specific goal, and added: "The fact that our society does admit the value of this kind of research and does support it, although somewhat feebly, is to my mind our best hope for peace and security."

Programmed research also is necessary, Prof. Hammett emphasized, but since its probable benefits are immediately apparent it wins support more easily. If government and industry are to increase their support for uncommitted research, he asserted, they must have the backing of an informed public opinion—and it is up to the scientists, who know the facts better than anyone else, to help the public develop an informed opinion.

Former President Harry S. Truman, who addressed a luncheon of the Division of Chemical Marketing and Economics, predicted that the next half-century would witness scientific developments as yet undreamed of. He expressed the wish that he could again be 20 years of age, instead of almost 70, so that he could see them. Mr. Truman praised scientists for their part in raising the world's living standard and urged them to continue studying the unknown for the benefit of mankind. He stressed the potentialities for world good in atomic energy and voiced the hope that neither the atom bomb nor the hydrogen bomb would ever again have to be used as a weapon.

Identification of a fourth abnormal form of hemoglobin in human red blood cells was among the advances reported in 697 technical papers. Harvey A. Itano of the California Institute of Technology, who received the Eli Lilly and Company Award in Biological Chemistry, announced the new hemoglobin in his award address. He and his colleagues, working under Prof. Linus Pauling, had previously traced the disease called sickle-cell anemia back to a defective hemoglobin and subsequently had identified two other abnormal forms of human hemoglobin. Their successes confirmed Prof. Pauling's theory that sickling—the occurrence of sickle-shaped red corpuscles—might result from an abnormality of the hemoglobin molecule. Prof. Pauling believes that some day such other maladies as heart disease and cancer may prove to be molecular in origin and thus susceptible to entirely new forms of treatment.

Progress in the study of the antibiotic azaserine, which is said to retard the growth of animal cancer, was described in a series of papers by chemists from the Sloan-Kettering Institute for Cancer Research; Parke, Davis and Company, and The Wellcome Research Laboratories. The antibiotic was reported to be particularly effective when used in combination with the compound 6-mercaptopurine. So far, preliminary clinical studies of azaserine in several forms of human cancer have not been impressive, according to C. Chester Stock, chief of Sloan-Kettering's experimental chemotherapy division, but researchers are hopeful that further studies will yield more encouraging results. In any event, he said, azaserine should prove a useful tool in learning more about the way cells grow.

Indications that cancer might be combated successfully through a combination of dietary control and chemotherapy were reported by James B. Allison, professor of physiology and biochemistry in Rutgers University, and associates. Studies now under way at Rutgers show that the life of a tumor-bearing animal may be prolonged through diet control, Prof. Allison said, and this may make it possible to use such chemicals as the triethylenimines to slow up, stop, or even cause regression of the cancer. Administration of T.E.P.A. (triethylenimino phosphoramide) to labora-

tory rats reduces food utilization in both normal and cancerous animals, it was stated. Daily use of T.E.P.A. in rats with experimental cancers caused the tumors—and all other tissues—to grow poorly. When the diet was supplemented with the amino acid methionine, however, the effect of T.E.P.A. on normal tissues was reduced while the tumor continued to be retarded.

A broad chemical attack is now under way against the disease-causing ameba known as *Endamoeba histolytica*, it was reported at a symposium of the Medicinal Division on the chemotherapy of amebiasis. The disease in one form or another is believed to afflict one person in every ten, according to E. C. Faust of Tulane University. He noted that although amebiasis is particularly prevalent in the tropics, its incidence rate also is high in temperate zone mental hospitals, prisons, children's homes, and rural areas. Several promising new amebicides were described.

The Medicinal Division also examined the current status of the chemical battle against helminths, or worms, in domestic animals which are costing farmers and pet owners more than $375,000,000 a year.

The curing of radiation injury in mice by means of a protective factor obtained from the nuclei of spleen cells was described by R. K. Main of the U.S. Naval Radiological Defense Laboratory, San Francisco, who termed the research "another step toward the ultimate goal of effective postirradiation treatment of radiation injury."

A new silicone molding compound that overcomes several critical limitations of present electrical insulation, and thus promises to increase the altitude and speed range of aircraft, was among the silicone developments announced at a joint symposium of the Divisions of Industrial and Engineering Chemistry and Paint, Plastics and Printing Ink Chemistry.

Advances in the fields of pesticides, synthetic detergents, synthetic liquid fuels and chemicals, and fuels for gas turbines and turbo-jet engines were surveyed by other divisions.

Registration totaled 3842 at the meeting, which as an experiment was held in two sessions. Eight divisions met from Wednesday through Saturday of the first week, and 11 other divisions from Monday through Thursday of the second week.

A highlight of the general assembly held on Saturday night of the first week was the announcement by ACS President Harry L. Fisher of the University of Southern California that the Society's Priestley Medal for 1954 had been awarded to W. Albert Noyes, Jr., chairman of the Department of Chemistry at the University of Rochester and editor of the *Journal of the American Chemical Society*. The medal will be presented at the Society's 126th national meeting in New York, Sept. 12–17.

WALTER J. MURPHY
American Chemical Society
Washington 6, D.C.

Science News

The **75th anniversary of the U.S. Geological Survey** was observed at a meeting on Apr. 21 sponsored by the Washington Society of Engineers in cooperation with the District Council of Engineering and Architectural Societies. W. E. Wrather, director of the Survey, assisted by members of his staff, presented a program briefly describing the history, functions, and activities of the bureau.

From a small group of able scientists, the Survey has grown to an organization of more than 6600 permanent employees. Its various activities were described at the meeting by Wilmot Bradley, chief geologist; Harold J. Duncan, chief, Conservation Division; Carl S. Paulsen, chief hydraulic engineer; Gerald Fitzgerald, chief topographic engineer; and Robert L. Moravetz, chief, Publications Office.

It is significant to note that, despite the age of the Survey, the present director is only the sixth person to hold that office. Previous directors are: Clarence King, 1879–1881; John Wesley Powell, 1881–1894; Charles D. Walcott, 1894–1907; George Otis Smith, 1907–1931; and Walter C. Mendenhall, 1931–1943.

As a part of its 5-yr **Coral Atoll Project**, which is supported by funds from the Office of Naval Research, the Pacific Science Board of the National Research Council will send a team to Kapingamarangi, Caroline Islands, in June. Members of the team will be: Edwin D. McKee, U.S. Geological Survey, Denver; Cadet Hand, University of California, Berkeley, marine; William A. Niering, Connecticut College, land ecologist; Robert R. Harry, George Vanderbilt Foundation, ichthyologist; Harold J. Wiens, Yale University, geographer; W. Jan Newhouse, University of Hawaii, algologist.

The coral atoll program, which is largely in the field of basic research and involves essentially an ecological approach to the study of environmental factors affecting life on coral atolls, is the principal activity under the Scientific Investigations in Micronesia program of the Board.

The case of a man who has been fighting **fluoridation** of his city's drinking water since December, 1951, is still pending on the docket of the U.S. Supreme Court. C. Leon de Aryan of San Diego holds that fluoridation violates the 4th and 10th amendments to the Constitution. Last November the California Supreme Court decided against him. Opponents of fluoridation will have an opportunity to voice their opinions in Washington, May 25–28, when hearings are scheduled for the Wier bill (HR 2341), which is to "protect the public health from the dangers of fluoridation of water."

Beginning with its April issue, *The Journal of Dental Medicine* will carry summaries of its articles in **Interlingua.** The *Journal* is the official organ of The American Academy of Dental Medicine and is under the editorship of Irving Yudkoff of New York.

A **"Proposal for a municipal laboratory center"** has been submitted to the Mayor of the City of New York by the New York Academy of Medicine. Embodied in this proposal is the recommendation:

"That there be established a Municipal Laboratory Center comprising the Public Health Research Institute, the Bureau of Laboratories of the Department of Health, the Air Pollution Control Laboratory, the contemplated Institute of Forensic Medicine, and possibly other laboratories whose work may be related. These units need not necessarily be housed in one building; instead, they could be separately located near each other."

Two studies of the **sickle-cell trait,** reported in the *British Medical Journal* for Feb. 6, 1954, have done much to clarify the perplexingly high incidence among Negroes of this hereditary blood condition, which in the homozygous condition produces a very serious anemia. According to genetic theory, even if the heterozygous condition is neutral, natural selection would be expected to reduce the frequency of the detrimental gene to a level in equilibrium with the mutation rate replenishing it in the population. Some geneticists have consequently postulated a very high mutation rate to account for the persistence of the gene among Negroes in Africa and N. America, although that explanation would require the corollary that in other racial groups the normal allele of the sickle-cell gene is not highly mutable but is quite stable.

A study made by Henry Foy, Athena Kondi, G. L. Timms, W. Brass, and Fardil Bushra of the presence of the sickle-cell trait in 7 tribes and subtribes of Kenya and the Southern Sudan shows that the frequency is extraordinarily variable. It was found to range from 0 to 40 percent. Even within subtribes, e.g., those of the Nyika of Kenya, it was not uniform, but ranged from 10 to 35 percent. Although these rates are based on relatively small samples, the differences are statistically highly significant. Of possible explanations for this variability, the authors suggest that genetic drift, that is, the effect in very small populations of random fluctuations in the transmission of genes from generation to generation, is the most likely.

A different explanation would seem to follow from the work of A. C. Allison, who found initially that in 290 Ganda children in East Africa infection with malarial parasites was 27.9 percent in the 43 children with sickling blood cells, but 45.7 percent in the 247 nonsicklers. He followed up this interesting observation by experimental infections of sicklers and nonsicklers. In some cases infection was by injection of the live parasites of tertian malaria, in others by being bitten by infected mosquitoes, and in the majority of cases by both routes. Out of 15 adult Luo natives without sickling, and a similar number of sicklers, all of whom were followed for 20 to 40 days before any infections that developed were stopped by chemotherapy, all but one of the nonsicklers became infected, whereas only 2 of the sicklers ever showed any signs of parasites and then only mildly and sporadically. It therefore seems quite certain that individuals with the sickle-cell trait are to a considerable degree more immune to tertian malaria than are nonsicklers. Selection in areas where malaria is endemic would thus tend to strike an equilibrium between the adverse effects of malaria and the adverse effects of sickle-cell anemia. This of course would not exclude in addition the operation of genetic drift, because of the small size of the mating groups in the African populations—B.G.

Project SQUID, a cooperative venture in science which has been proceeding quietly for 8 yr, is a joint effort on the part of the Army, the Navy and the Air Force to foster basic research in those fields that relate to jet propulsion of aircraft. With funds provided by the Office of Naval Research, the Office of Scientific Research of the Air Force, and the Office of Ordnance Research of the Army, SQUID has been harvesting new knowledge in heat transfer, fluid mechanics, and combustion. Universities having subcontracts on Project SQUID have encouraged graduate students to participate in the program. As a result, approximately 350 student years of graduate employment training have been provided.

The administrative structure of Project SQUID is somewhat unique. It comprises a prime contract between the Office of Naval Research and Princeton University. Princeton, in turn, lets subcontracts with other university and corporate laboratories. Altogether there are three companies, eleven universities, and one government laboratory in the program. In terms of high government finance, SQUID operates with a minuscule budget. Moreover, it imposes no hardware commitments upon its participants. Its efforts are directed largely at the pursuit of basic information. Nevertheless, in addition to over 200 technical reports and publications, it has given birth to important practical developments that are now contemplated for operations use.

On Mar. 17–19 SQUID personnel from all over the country met in Princeton to report their progress for the preceding year and to exchange ideas that will make tomorrow's planes and missiles outperform today's models.

The main text of the report of a committee of the American Statistical Association, appointed in 1950 to review **the statistical methods employed by A. C. Kinsey, W. B. Pomeroy, and C. E. Martin** in their *Sexual Behavior in the Human Male,* has been published in the December, 1953, issue of the *Journal of the American Statistical Association.* The authors of the report, William G. Cochran of Johns Hopkins University, Frederick Mosteller of Harvard University, and John W. Tukey of Princeton University, hold that in investigating their very complex problem, Kinsey and his colleagues handled some aspects admirably and failed to handle others adequately. Their over-all impression of the work is favorable. In comparison with other leading sex studies, "the statistical and methodological aspects of KPM's work are outstand-

ing. . . ." In making their interpretations, however, not only were these in part based on the tabulated and statistically analyzed data, but also in part on data or experience that were not presented; and the interpretations therefore sometimes appear to be unsubstantiated assertions. "Many of KPM's findings are subject to question because of a possible bias in the constitution of the sample. This is not a criticism of their work (although it is a criticism of some of their interpretations)." The committee adds that many of the Kinsey findings are subject to question because of possible inaccuracies of memory and report, as in all such studies. No one has proposed any way to avoid this, but it must always be kept in mind that this is *reported* behavior. The committee feels that the Kinsey group received too little statistical help, partly because of wartime conditions; and the present need for additional aid of this kind remains great. The sort of assistance they require is of a type that "perhaps not more than twenty statisticians in the world possess."

The committee recommends that the Kinsey group should seriously consider a probability sampling program, at least in the form of a small pilot study. Numerous other suggestions were made, such as the expansion of "methodological checks of their sampling program, a further study of their refusal rate, some modification of their methods of analyses, further comparisons of reported vs. observed behavior, and stricter interpretations of their data." Some of these recommendations are stated by Kinsey's group to have been utilized already in the book on sexual behavior in the human female. [Others obviously were not, in particular the recommendation to include at least a small probability sample.]

In comparison with nine other leading sex studies, "KPM's work is outstandingly good. . . . Their interviewing ranks with the best, they have more and better checks, their geographic and social class representation is broader and better, their volunteer nonprobability sample problem is the same, they have used more varied and searching methods of analysis, [and] only two of the nine studies (Davis and Farris) were more careful about generalization and warned the reader more thoroughly about its dangers." As to the four major controversial findings of the Kinsey group, namely, (1) the high general rate of sexual activity, including homosexuality, (2) the slight change from the older to the younger generations (3) the strong relation between activity and socio-economic class, and (4) relations between activity and *changes* of socio-economic class—all of which were set forth as well-established conclusions—the committee warns that "all are subject to unknown allowances for (*a*) difference between reported and actual behavior, [and] (*b*) nonprobability sampling involving volunteering. While their findings may be substantially correct, it is hard to set any bounds within which the truth is statistically assured to lie. . . . The same difficulties are present in many sociological investigations."—B.G.

More than 24,000 specimens of plants, including some hitherto unknown to science, have just been brought back to the Smithsonian Institution by A. C. Smith, a curator of the U. S. National Museum, after a 9-mo collection trip in the Fiji Islands. This was Dr. Smith's third trip to Fiji, and during it he concentrated on four of the larger islands, Viti Levu, Ovalau, Ngau, and Taveuni, in an effort to obtain representative collections from previously neglected areas. Fiji is of especial interest to botanists because it appears to represent the eastern rim of an ancient land mass that presumably extended westward from Fiji to Indo-Malaysian regions. This so-called Melanesian continent is supposed to have been disrupted approximately 10 or 20 million years ago, since which time its present remnants have been isolated from one another. These modern archipelagoes, including not only Fiji but also the New Hebrides, the Solomons, and New Caledonia, are in effect refuges where a great number of distinct species have evolved. New Guinea was apparently the center from which much of the plant life spread eastward.

At least one Fijian plant, the degeneria, suggests that portions of the Melanesian region have been above the sea since the first flowering plants appeared on earth, conceivably more than 100 million years ago. The degeneria is a tall forest tree with beautiful white flowers, first discovered by Dr. Smith 20 yr ago and since discovered in many parts of Fiji. In many respects it is among the most primitive extant flowering plants suggesting, but differing from, the magnolia family, itself a supposedly primitive group. Another striking Fijian plant is the tangimauthia, a climbing vine with beautiful red, white, and blue inflorescences, known only on the summits of two islands. While collecting this rarity, Dr. Smith found growing with it a new and equally spectacular plant of the same genus, technically known as Medinilla.

Scientists in the News

George A. Boyd has resigned as professor of biophysics at the University of Tennessee and as senior scientist for the Oak Ridge Institute of Nuclear Studies to accept directorship of the Arizona Research Laboratories, Phoenix, Ariz. This is a new industrial research laboratory that has grown out of the 22-yr-old Arizona Testing Laboratories. It is a division of Claude E. McLean & Son Laboratories, Inc., and will conduct arid zone research.

Karl T. Compton, chairman of the corporation of the Massachusetts Institute of Technology, has been elected chairman of a 12-member New England committee that will study the use of atomic energy for peacetime purposes in the northeastern part of the country. The committee was named by Gov. John Davis Lodge of Connecticut in his capacity as chairman of the New England Governors Conference.

Kenneth B. M. Crooks, formerly professor of biology at the Hampton Institute and since 1941 headmaster of Happy Grove College, Jamaica, is serving

during a year's leave of absence as a professor of zoology at the State College in Fort Valley, Ga.

Ira V. Hiscock, professor of public health at Yale University School of Medicine, has received the 1954 Shattuck Award of the Massachusetts Public Health Association for outstanding contributions to the field of public health. He has also received the 1954 Medal of the Connecticut Division of the American Cancer Society and, in addition, has been elected president of the Association of Schools of Public Health of the United States and Canada.

John Oliver La Gorce, vice president and associate editor of the National Geographic Society and a member of the organization's staff for nearly 49 yr, has been elected president and editor. He was nominated by the man he succeeds, **Gilbert Grosvenor,** who is retiring after more than 55 yr of service. Dr. Grosvenor's resignation was accepted only on the condition that he become chairman of the Board of Trustees, and he was elected unanimously to that position.

The Society has also announced that **Melville Bell Grosvenor,** Dr. Grosvenor's son and long the senior assistant editor, has been elected vice president and associate editor. Thomas W. McKnew is secretary of the Society, and Robert V. Fleming, president of the Riggs National Bank, is treasurer.

John R. Pellam, chief of the Cryogenic Physics Section of the National Bureau of Standards, has been appointed professor of physics at the California Institute of Technology, effective July 1.

On May 1, **William G. Pollard,** physicist and director of the Oak Ridge Institute of Nuclear Studies, was ordained as an Episcopal priest. Dr. Pollard plans to continue in his present post.

The following awards were made at the 125th national meeting of the American Chemical Society in Kansas City, Mar. 24–Apr. 1:

John D. Roberts of California Institute of Technology, the ACS Award in Pure Chemistry.

Donald V. Josephson of Pennsylvania State University, the Borden Award in the Chemistry of Milk.

G. Frederick Smith of University of Illinois, the Fisher Award in Analytical Chemistry.

A. R. Penfold of Sydney Technological Museum, the Fritzsche Award.

Betty Sullivan of Russell Miller Milling Company, Minneapolis, the Garvan Medal.

Harry N. Holmes professor emeritus of Oberlin College, the Kendall Company Award in Colloid Chemistry.

Harvey A. Itano of California Institute of Technology, the Eli Lilly Award in Biological Chemistry.

Alton Meister of National Cancer Institute, the Paul-Lewis Laboratories Award in Enzyme Chemistry.

Arthur Lien of Standard Oil (Ind.), the Precision Scientific Company Award in Petroleum Chemistry.

Raymond E. Kirk of Polytechnic Institute of Brooklyn, the Scientific Apparatus Makers Award in Chemical Education.

Homer L. Shantz, internationally known plant geographer, has received the Outstanding Achievement Award for 1953 of the Association of American Geographers. Dr. Shantz, retired chief of the wildlife management division of the U.S. Department of Agricultural and now living in Santa Barbara, Calif., was cited "for his contribution to geographic understanding of vegetation types in relation to soil and agriculture, especially in the United States and Africa." He is best known as the author of the Agriculture Department's map of vegetation types in the United States, regarded by botanists and geographers as a monumental work.

Presentation of the award was made on Apr. 14 at a dinner climaxing the AAG's 50th anniversary meeting in Philadelphia. In addition, citations for meritorious contributions to the field of geography were awarded to:

James W. Watson of Ottawa, director of the geographic branch of the Canadian Department of Mines and Technical Surveys, "for distinguished services in the establishment of a geographic office in the Canadian Government and for original contributions to the historical geography of settlement in Ontario."

Raymond E. Murphy, professor of economic geography at Clark University, "for outstanding success in bringing to *Economic Geography* (as its editor) broad professional support and a high degree of editorial excellence."

Francis J. Marschner, agricultural economist of the U.S. Department of Agriculture, "for contributions to our knowledge of land utilization and particularly for his fundamental land-use map of the United States."

William S. Stone, director of the graduate school at Walter Reed Medical Center in Washington, has been named director of medical research and education at the University of Maryland. He will be in charge of both the School of Medicine and University Hospital in Baltimore. H. Boyd Wylie continues as dean of the School of Medicine and George H. Buck continues as director of the hospital.

Horace W. Stunkard, chairman of the graduate and undergraduate divisions of biology at the University Heights campus of New York University, will retire in September. **Charles H. Willey,** professor of biology, succeeds him as head of undergraduate biology. **Harry A. Charipper,** chairman of the Department of Biology on the Washington Square campus, will continue in that post and in addition will direct the graduate departments of biology for both campuses.

Dr. Stunkard plans to continue his experimental studies into the life cycles of parasitic flatworms, especially those found in the bloodstream. Among his

works in this field was his investigation during World War II of the life history of schistosomiasis, a blood disease occurring primarily in the Far East. Serving as consultant to the Office of Scientific Research and Development, he studied thousands of snails and found a species capable of harboring the larval stages of the flatworm that causes the disease. In another project extending over several years, Dr. Stunkard was the first to identify the salt-water form of a cercarial parasite responsible for the dermatitis experienced by bathers and known commonly as "swimmer's itch." His research into the life history and development of the parasitic worm Cryptocotyle lingua, which attacks the intestine, brought him the A. Cressy Morrison prize for research of the New York Academy of Sciences in 1929. In all, Dr. Stunkard has experimented on the complicated life cycles, successive larval stages, and methods of transmission from one host to another of 14 parasitic organisms, 10 trematodes, and 4 cestodes. He has directed graduate students at NYU in tracing the cycles of 19 more parasites.

Dr. Stunkard was educated at Coe College, Cedar Rapids, and received his M.S. and Ph.D. degrees from the University of Illinois. He taught at Illinois before joining NYU as a biology instructor in 1916. Coe College presented the honorary doctor of science degree to him in 1937. On occasional leaves from NYU, Dr. Stunkard has conducted research in marine biology and tropical diseases in England, France, and Germany. He is a member of 18 scientific societies and is author of 144 scientific papers and reviews. Earlier this year he retired as editor of the *Journal of Parasitology*, a post he held for 10 yr. He is a vice president of the AAAS and chairman of Section F—Zoological Sciences; he is president of the Society for Systematic Zoology and past president of the American Society of Parasitologists, the American Microscopical Society, and the New York Society for Tropical Medicine.

Thomas H. Weller, virologist and parasitologist and a leading investigator in the field of poliomyelitis, has been made Richard Pearson Strong professor of tropical public health at the Harvard School of Public Health. Dr. Weller is the first incumbent in the first endowed professorial chair at the School. Endowment funds for the professorship were raised by friends and colleagues of the late Dr. Strong, a professor of tropical medicine at Harvard and a pioneer in tropical research, and included a gift of 1,000,000 francs from the Belgian Government and a gift of 1000 pesos from a group of health officials and employees of the government of the Republic of the Philippines.

Edwin A. Wiggin, formerly chief of the Technical Developments Branch of the Atomic Energy Commission's Isotopes Division in Oak Ridge, has been named manager of technical information of the Atomic Industrial Forum, Inc., New York. Mr. Wiggin will supervise the Forum's dissemination of technical information and will oversee the Forum's library, which was recently designated by the AEC as the first off-project depository of industrial information.

William F. Windle, previously scientific director of the Baxter Laboratories, Morton Grove, Ill., is now chief of the Laboratory of Neuroanatomical Sciences of the National Institute of Neurological Diseases and Blindness, U.S. Department of Health, Education, and Welfare.

Hideki Yukawa, 1949 Nobel prize winner in physics and professor at Columbia University, has resigned, effective in June, to return to the University of Kyoto, Japan, where a research institute has been named for him.

Education

The Harvard Medical School and the Peter Bent Brigham Hospital have announced the opening of the **Biophysics Research Laboratory of the Department of Medicine at the Peter Bent Brigham Hospital.** The chief interest of the laboratory is the study of the "trace elements" in biology and medicine. The laboratory is equipped for work in biophysics, biochemistry, and physical chemistry. Among the facilities for instrumental analysis, spectrographic equipment is emphasized. Biochemical and biophysical approaches will be combined wherever possible. Training facilities are provided for pre- and postdoctoral students in the natural sciences and medicine. The laboratory, which has been constructed over a period of 3 yr, has a floor area of about 8000 ft^2. It is staffed by Bert L. Vallee and his associates—Frederick L. Hoch, Marvin Margoshes, and Ralph E. Theirs.

The **Colorado School of Mines,** Golden, is offering two summer field courses—one at Wild Horse Park in geology, June 1–July 10; and one at Aspen in mining geology, Aug. 3–Sept. 11.

This summer the University of Texas will open an **Institute for Advanced Engineering** that will offer practicing engineers opportunities for short-course briefings on professional advances which have taken place since they were graduated. The College of Engineering will conduct the Institute with the cooperation of the Division of Extension. Three courses will be offered, each lasting 3 wk: "Advanced experimental stress analysis," June 14–July 2; "New developments in communication theory," Aug. 16–Sept. 3; and "Composition and properties of oil well drilling fluids," Aug. 26–Sept. 15.

The Institute plans to offer courses in various fields throughout the year when demand justifies. Studies will emphasize mathematical and scientific theories leading to new discoveries and the implications and applications of such theories in engineering and applied science. Fields in which courses may be conducted include petroleum production and refining, chemical synthesis, radar and other electronics, nuclear reactions, structural and building technology ap-

plied to warmer climates, aeronautical and engineering mechanics theories involving supersonic stresses, and solar energy.

The **Institute of Silicate Research** at the University of Toledo was dedicated on May 15. The laboratories include a two-story furnace hall for high-temperature work and facilties for research in physical chemistry, colloid chemistry, x-rays, microphotography, microscopy, refractometry, interferometry, and so on. Considerable equipment from other departments of the university also is available for use.

The institute is a unique center for basic research and for the education of pure scientists and research engineers. It is supported by the university and five nationally known firms—the Libbey-Owens-Ford Co., Owens-Corning Fiberglas Corp., Owens-Illinois Glass Co., Pittsburgh Plate Glass Co., and Columbia-Southern Chemical Corp. Wilhelm Eitel is director of the institute, which has been in the process of development for nearly 2 yr.

A 4-yr program in **medical technology** has been inaugurated by Elmira College, Elmira, N.Y., in conjunction with the Arnot-Ogden Memorial Hospital. Following 3 yr of basic training at the college and 12 mo of instruction at the hospital, a student will be granted a B.S. degree by Elmira; then, upon successful completion of an examination offered by the Registry of Medical Technologists, he will be issued a certificate in Medical Technology by the Registry of Medical Technologists of the American Society of Clinical Pathologists.

A **new soil-testing laboratory** in Marianna, Ark., the Eastern Arkansas Branch Laboratory of the Cotton Branch Experiment Station, Fayetteville, will be formally dedicated on June 10. Assistant Secretary of Agriculture J. Earl Coke and Governor Francis Cherry will participate in the ceremony. The laboratory will serve the farmers in 26 counties of eastern Arkansas; the remaining counties will continue to use the Main Laboratory. The new branch will be under the supervision of Richard Maples, a member of the Agronomy Department who was formerly stationed at Fayetteville.

Formal acceptance of the Columbus Cancer Clinic as a part of the Cancer Wing of University Hospital has been voted by the Board of Trustees of the **Ohio State University.** Facilities and functions of the Clinic, including the General Populace Clinics, will be moved gradually to their new location on the first floor in the north wing of University Hospital. Completion of the shift is expected by Sept. 1.

Last year the nation's 79 medical schools operated at an estimated deficit of $10,000,000, said A. C. Furstenberg, dean of the University of Michigan Medical School, in the Edward and Susan Lowe Fellowship Lecture given in Grand Rapids recently. In the past 10 yr, teaching budgets have increased 94 percent; administration, 116 percent; and plant operation, 45 percent. And although tuition fees have risen 165 percent since 1940, they still provide only one-fifth of the total costs of a medical education.

It has reached the point of a national crisis, the dean stated, and he added that "Unless support is forthcoming from some source, many medical schools will be forced to lower their standards of training or close their doors entirely."

Industrial applications of atomic energy will be covered in a 2-wk short course at Purdue University, from July 12–23. Similar in objectives to instruction offered by the Oak Ridge Institute of Nuclear Studies, this will be the first intensive short course offered by any university. It is designed to aid in meeting an acute shortage of trained personnel in the field of **radiochemistry.**

William H. Johnston, of the Chemistry Department, will be in charge of the course; during the war he worked on the plutonium bomb. He will be assisted by George Goldsmith of the Physics Department, who is associated with Karl Lark-Horovitz in the extensive solid-state research program which has made major contributions to the recent development of the transistor.

The course will cover the basic principles of radiochemistry, the design of experiments, instrumentation, and applications to industry. Among those participating as instructors will be James R. Arnold of the Institute of Nuclear Studies at the University of Chicago; Joseph Kennedy, head of the Chemistry Department at Washington University, who during the war was director of the Chemical Division at Los Alamos; and representatives of the Atomic Energy Commission.

Grants, Fellowships, and Awards

The **American Heart Association** has announced that the **Howard W. Blakeslee Award** for outstanding scientific reporting in the field of heart and blood vessel diseases will be divided into several awards to cover specific categories of newspapers, periodicals, radio, and television, instead of the single award established last year. The exact number of awards and the categories from which the winners will be selected by the judges are to be determined at a later date.

It was decided to increase the number of awards because of the general excellence of the entries in the major areas of mass communication. The awards will provide a minimum of $500 for each category to be selected by the judges, rather than the original single honorarium of $1000. Additional funds for this purpose have been made possible through the generosity of Frank N. Isbey, a member of the Association's Board of Directors. His contribution supplements funds already made available by the Eva and Irving Hexter Foundation of Cleveland and the Robert Z. Greene Foundation of New York. The Blakeslee Award was established last year in memory of Howard W. Blakeslee, the late science editor of the Associated

Press and founder of the National Association of Science Writers, who died of heart disease.

To assist scientists in carrying out part of their research program in Bermuda, a generous grant covering a period of 5 yr has been made to the **Bermuda Biological Station** by the National Science Foundation. These funds, which are immediately available, will be awarded mainly to pay for research space, living expenses, or special collecting facilities required at the station. Applications for aid in purchasing equipment or for necessary travel expenses may also be considered in relation to such a program.

A booklet describing the particular advantages and facilities of the Bermuda Biological Station, as well as application forms for the fellowships, are available from the director, Dr. William H. Sutcliffe, Jr., Bermuda Biological Station, St. George's West, Bermuda. *Application should be made as soon as possible.*

The **Department of Microbiology of the Tulane University School of Medicine** will have available one or two graduate assistantships paying approximately $1000–$2000 for the next academic year. The assistantships, which are intended for students working toward the Ph.D. degree, will involve participation in the research programs of the department. Candidates should have a good background in chemistry.

The deadline for filing applications is June 30. Further information may be obtained from the Chairman, Department of Microbiology, Tulane University, New Orleans 18, La.

Eli Lilly and Company, Indianapolis, has recently awarded the following research grants:

California Institute of Technology. H. Borsook, Kerchoff Laboratories. Synthesis of a variety of fructosyl compounds.

University of California. I. L. Chaikoff, School of Medicine. Mechanisms of insulin's action.

Duke University. F. L. Engel, School of Medicine. Carbohydrate metabolism.

Florida State University. H. M. Walborsky, Dept. of Chemistry. Total synthesis of carbohydrates.

Johns Hopkins University. F. B. Bang, Dept. of Parasitology. Chemotherapy of schistosomiasis.

Johns Hopkins University. S. R. M. Reynolds and R. Te Linde, Dept. of Gynecology. Physiological conditions in and pharmacological responses of the nongravid human cervix uteri.

Massachusetts Institute of Technology. G. Buchi, Dept. of Chemistry. Chemical structure of aconite alkaloids.

Purdue University. C. L. Porter, Dept. of Biological Sciences. Antibacterial and antiviral activities of certain microorganisms.

St. Louis College of Pharmacy and Allied Sciences. A. G. Zupko, Dept. of Pharmacology. Anhydrotic and antisialogogue effects of "Elorine Sulfate."

Vanderbilt University. A. D. Bass, Dept. of Pharmacology. Effect of alloxan diabetes on liver nucleic acids.

McGill University, Montreal. K. I. Melville, Dept. of Pharmacology. Possible significance of nutritional and hormonal factors in affecting responsiveness of coronary circulation to drugs; *in vitro* effects of various types of coronary drugs on the metabolism of surviving coronary arterial strips.

Royal Victoria Hospital, Montreal. B. Rose, University Clinic. Antibodies related to sensitivity phenomena.

University College of the West Indies, Jamaica. C. H. Hassall, Dept. of Chemistry. Hypoglycin A and B.

Two graduate assistantships in pharmacognosy are available at the University of Pittsburgh School of Pharmacy beginning with the fall term. Each assistantship involves 10 mo of service during which the recipient will be expected to engage in part-time teaching. Graduate students in pharmacognosy will supplement their training in that field with elective courses in plant physiology, plant chemistry, plant anatomy, or related fields. Applicants interested in study of allergenic plants will have an excellent opportunity to follow this specialty.

Graduate courses leading to the M.S. degree in either pharmacognosy or pharmacology and to the Ph.D. degree in pharmacy are being offered. Interested persons should communicate with the Dean, University of Pittsburgh School of Pharmacy, Pittsburgh 19, Pa.

The **Institute of Air Flight Structures at Columbia University** is offering Daniel and Florence Guggenheim fellowships, in amounts up to $2000, for graduate study in the field of air flight structures for sonic and supersonic planes and rockets. Applicants are not required to have a degree in aeronautical engineering, but are expected to have a bachelor's degree in some branch of engineering or physical science from an accredited institution. Fellowships are renewable.

After 2 yr of graduate study as a Guggenheim fellow, students have essentially completed their course of work and are ready to become members of one of the research teams active at the Institute. They may write their doctoral thesis on the subject of this research. Principal faculty members assigned to the Institute, which is in the School of Engineering, are Hans H. Bleich, director; Lee Arnold; Alfred M. Freudenthal; and Bruno A. Boley.

The **National Science Foundation** has awarded 79 1-yr postdoctoral fellowships for advanced study and research in the natural sciences for the academic year 1954–55. These postdoctoral fellowship recipients were selected from 461 applicants and are in addition to the 657 predoctoral fellowships announced earlier. Last year, 42 postdoctoral fellows were selected from 368 applicants and for the academic year 1951–52, 55 fellows were selected from 292 applicants. Of the current awards, 36 are in the life sciences, 15 in chemistry, 13 in physics and astronomy, 12 in mathematics, 2 in the earth sciences, and 1 in engineering.

Alabama

J. C. O'Kelley, Tuscaloosa; Iowa State Coll., Bot.

Arizona

W. V. F. Brooks, Tucson; U. of Minnesota, Chem.

California

R. C. Blanchfield, S. Pasadena; Princeton U., Math. Sci.
M. J. Cohen, Los Angeles; U. of California, Zool.
J. W. Durham, Berkeley; U. of California, Earth Sci.
R. E. Glick, Sherman Oaks; U. of California, Chem.
D. L. Glusker, Santa Monica; Oxford U., Chem.
R. F. Heck, Los Angeles; U. of California, Chem.
J. A. Ibers, Pasadena; California Inst. of Tech., Chem.
L. F. Jaffe, Pacific Grove; Hopkins Marine Station, Bot.
J. A. Lockhart, Los Angeles; U. of California, Bot.
P. C. Martin, Los Angeles; Harvard U., Phys.
L. Ordin, Berkeley; U. of California, Bot.
D. D. Perkins, Stanford; Columbia U., Gen.
D. M. Prescott, Berkeley; U. of California, Zool.
E. Reich, Santa Monica; U. of California, Math. Sci.

W. G. Sly, Lakeside; California Inst. of Tech., Chem.
M. D. Van Dyke, Los Altos; California Inst. of Tech., Eng.

Colorado

J. L. Westley, Denver; U. of Chicago, Gen.

Connecticut

H. M. Dintzis, New Haven; Yale U., Biochem.
W. S. Hillman, Westport; Yale U., Bot.
W. C. G. Ortel, New Haven; Yale U., Phys.
F. M. Richards, Wilton; Harvard U., Biochem.
I. Tessman, New Haven; Yale U., Phys.

District of Columbia

F. S. Ham, Washington, D. C.; Harvard U., Phys.

Florida

E. F. Cox, Bradenton; California Inst. of Tech., Chem.

Illinois

V. R. Dorjahn, Evanston; Northwestern U., Anthrop.
W. E. M. Lands, Urbana; U. of Illinois, Biochem.
R. W. Lichtwardt, Champaign; U. of Illinois, Bot.
E. R. Rich, Chicago; U. of Chicago, Gen. Biol.
J. G. Wegener, Chicago; U. of Chicago, Psych.

Indiana

W. M. Huebsch, South Bend; U. of Notre Dame, Math. Sci.

Iowa

W. H. Orgell, Hubbard; U. of California, Bot.

Maryland

H. L. Plaine, Baltimore; Johns Hopkins U., Gen.

Massachusetts

P. S. Chen, Jr., S. Lancaster; U. of Rochester, Med. Sci.
T. Delevoryas, Chicopee Falls; U. of Illinois, Bot.
W. B. Hawkins, Jr., Springfield; Princeton U., Phys.
M. Karplus, W. Newton; Oxford U., Chem.
H. W. Kendall, Sharon; M.I.T., Phys.
J. H. Luft, Boston; Peter Bent Brigham Hospital, Zool.
D. M. Maynard, Jr., W. Newton; U. of California, Zool.
J. C. Moore, Belmont; Princeton U., Math. Sci.
B. B. Stowe, Cambridge; Harvard U., Bot.
L. Wilets, Auburn; Inst. for Theoretical Physics, Copenhagen, Phys.

Michigan

E. Weiss, Ann Arbor; M.I.T., Math. Sci.

Minnesota

G. E. Baxter, Minneapolis; U. of Minnesota, Math. Sci.
D. T. Lykken, Minneapolis; U. of Minnesota; Psych.

Missouri

S. G. Bradley, Springfield; Northwestern U., Microbiol.
K. L. Rinehart, Jr., Chillocothe; U. of California, Chem.

Nebraska

M. F. Ruchte, Lincoln; U. of Wisconsin, Math. Sci.

New Jersey

G. L. Bate, Bergenfield; Columbia U., Earth Sci.
G. S. Bernstein, Trenton; U. of Delaware, Biochem.
D. A. Buchsbaum, Princeton; Columbia U., Math. Sci.
V. L. Shapiro, New Brunswick; Inst. for Advanced Study, Math. Sci.

New York

L. N. Cooper, Great Neck; Columbia U., Phys.
G. F. Endres, Brooklyn; Polytechnic Inst. of Brooklyn, Chem.
G. Felsenfeld, New York; California Inst. of Tech., Chem.
R. C. Lewontin, Flushing; Columbia U., Gen.
A. P. Mattuck, Brooklyn; Princeton U., Math. Sci.
A. Roberts, Rochester; U. of Rochester, Phys.
D. Rogers, Buffalo; Oregon State Coll., Biochem.

Ohio

G. E. Briggs, Briggsdale; U. of Wisconsin, Psych.
K. T. Brown, Yellow Springs; U. of Chicago, Psych.
J. B. Hendrickson, Toledo; Harvard U., Chem.
K. G. Henize, Cincinnati; U. of Michigan, Astron.
C. H. Southwick, Wooster, U. of Wisconsin, Zool.

Oklahoma

W. C. Hamilton, Stillwater; California Inst. of Tech., Chem.

Pennsylvania

L. N. Castor, Jr., Philadelphia; U. of Pennsylvania, Zool.
J. Feldman, Philadelphia; Columbia U., Math. Sci.
W. L. Fite, Jenkintown; Harvard U., Phys.

Texas

G. L. Webster, Cedar Valley; Harvard U., Bot.

Washington

B. A. Campbell, Seattle; Yale U., Psych.

Wisconsin

W. L. Culberson, Madison; U. of Wisconsin, Bot.
C. W. Curtis, Madison; Yale U., Math. Sci.
J. F. Horning, Milwaukee; U. of Wisconsin, Chem.
R. E. Ireland, Madison; U. of Wisconsin, Chem.
W. E. Johnson, Osseo; U. of Wisconsin, Zool.
M. Tinkham, Ripon; M.I.T., Phys.

Wyoming

R. E. Cutkosky, Cheyenne; Carnegie Inst. of Tech., Phys.

The **National Research Council of Canada** has granted 236 scholarships for 1954–55, with a total value of $283,200. These scholarships include 75 bursaries of $800 each, 103 studentships of $1100 each, and 21 fellowships of $1400 each. All of these are to be held in Canada.

Special scholarships for study abroad include 20 $1900 awards that are to be held in the following countries: 10 in the United States, 8 in the United Kingdom, 1 in France, and 1 in Sweden.

Seventeen overseas postdoctorate fellowships at $2500 each have been granted for work in the following countries: 12 in the United Kingdom, 2 in Sweden, and 1 each in Denmark, in France, and in the Netherlands.

The **Theobald Smith Award** of $1000 and a bronze medal, which has been given yearly since 1937 (except for a lapse during the war years) by Eli Lilly and Company of Indianapolis, under the auspices of the AAAS, will be presented at the Association's 121st Meeting in Berkeley, Dec. 26–31.

Nominations for the award may be made by Fellows of the AAAS and should be sent *before Sept. 1* to the Secretary of the Section of Medical Sciences, Dr. Allan D. Bass, Department of Pharmacology, Vanderbilt University School of Medicine, Nashville 5, Tenn. Nominations should be accompanied by six copies of a statement giving full information concerning the nominee's personality, training, and research work.

The prize is given for "demonstrated research in the field of the medical sciences, taking into consideration independence of thought and originality." Any U.S. citizen who was less than 35 yr of age on Jan. 1, 1954, is eligible. The research is not to be judged in comparison with the work of more mature and experienced investigators. The vice president of Section N and four Fellows will form the committee of award.

Two new fellowships in biochemistry have recently been established at **Yale University School of Medicine.** Through the generosity of two alumni, it has been possible to establish the Lafayette B. Mendel Fellowship in Biochemistry, for exceptionally promising first-year graduate students. The first award will be made this

spring. In addition, the Lalor Fellowship in Biochemistry, for predoctoral graduate students, has been made possible by a gift from the Lalor Foundation.

Meetings and Elections

The **37th Annual Conference and Exhibition of The Chemical Institute of Canada** will be held in Toronto, June 21–23. Some 1200 delegates are expected to attend. A special feature will be a symposium on the chemical engineer in Canada.

The **Association of American Geographers** has elected the following officers: pres., Joseph A. Russell, Department of Geography, University of Illinois; v. pres., Louis O. Quam, Office of Naval Research; sec., Burton W. Adkinson, Reference Department, Library of Congress.

The spring meeting of the **Committee for the Scientific Study of Religion** was held in New York on Apr. 10. Featured on the program was a panel discussion on the subject "What do we know about the relation between religious beliefs, behavior patterns, and attitudes to behavior in secular activities?" Participants were Charles Y. Glock and Horace Friess of Columbia, Richard V. McCann of Harvard, Arthur L. Swift, Jr., of Union Seminary, and Robert Knapp of Wesleyan and the Ford Foundation.

The date for the fall meeting at Harvard University was set for Nov. 6. The program is to be divided between reports on empirical investigations and presentations concerning theories and techniques. Those who have papers of not over 20 min to propose should send two copies of a 300-word abstract to Prof. Richard B. McCann, 48 Mt. Auburn St., Cambridge 38, Mass., *before Sept. 30.*

Scholars having research projects in the field of the scientific study of religion to be endorsed by the Committee should send 10 copies of a description not exceeding 1000 words, together with a curriculum vitae, to Mr. Ralph Burhoe, American Academy of Arts and Sciences, 28 Newbury St., Boston, at least 6 wk before the deadline set for the call for papers for any particular meeting. If approved by the Executive Committee and its advisors, the proposer will be asked to supply mimeographed copies of his proposal to be circulated among the membership; he will also be asked to appear at the meeting to defend his project. At this time the membership will vote on the question of approval. The fee to cover expenses will be $10, payable with the initial submission of material. For further information about the Committee, write the secretary, Dean W. H. Clark, Hartford School of Religious Education, Hartford 5, Conn.

Forty-four outstanding researchers recently participated in a 2-day conference on **"6-Mercaptopurine"** that was held under the auspices of the New York Academy of Sciences. In organizing the conference, the cochairman, George H. Hitchings of the Wellcome Research Laboratories, Tuckahoe, N.Y., and C. P. Rhoads of the Memorial Hospital Center for Cancer and Allied Diseases, New York, brought together the leading scientists in the various laboratories and hospitals in this country and from France and the Argentine to bring up to date the work that has been done with 6-Mercaptopurine and the results obtained in its use.

Recent studies of drug effects on mental disorders, latest progress in the chemical attack on hardening of the arteries, and the role of pituitary hormones in the body are three of the topics to be discussed at the **4th National Medicinal Chemistry Symposium**, to be sponsored by the American Chemical Society's Division of Medicinal Chemistry at Syracuse University, June 17–19. Amel R. Menotti of Bristol Laboratories, Inc., Syracuse, is chairman of the symposium and Thomas P. Carney of Eli Lilly & Company, Indianapolis, is program chairman. Charles F. Kettering, dean of American automotive engineers and inventor of the first successful electric self-starter, will present the main address at the symposium banquet June 17.

Certain aspects of the digestive process will be discussed at the opening session at which Alfred Burger, chairman of the Division, will preside. Robert R. Burtner of G. D. Searle & Company will explain the chemistry involved in a study of the problem, and Joseph Webb of the Upjohn Company will report on the action of drugs and natural factors.

Chemical substances that attack atherosclerosis will be described by Robert Shipley of Eli Lilly & Company, and the parts played in atherosclerosis by cholesterol and lipoprotein will be discussed by R. Gordon Gould of the University of California and Douglas Surgenor of the Harvard Medical School. J. O. Lampen of E. R. Squibb and Sons will be chairman.

Alkaloids will be the topic of the session conducted by Chester Cavallito of the Irwin-Neisler Company. Dr. Cavallito will survey the importance of alkaloids in medicinal chemistry, Bernhard Witkop of the National Institute of Arthritis and Metabolic Diseases will describe modern methods for certain studies of alkaloids, and Leo Marion of the National Research Council of Canada will discuss the formation of alkaloids in living organisms.

Vincent du Vigneaud of the Cornell University Medical College, leader of the team of chemists that synthesized the pituitary hormone oxytocin last year, will report on this work and the activities of hormones produced by the posterior section of the pituitary gland. Oxytocin, an important factor in childbirth and lactation, is the first polypeptide hormone to be produced synthetically. Others to speak at this session are James Sprague of Sharp & Dohme, who will preside, and Klaus Hofmann of the University of Pittsburgh School of Medicine.

A panel discussion will be conducted on "Mechanism of drug action," under the guidance of Bernard Brodie of the National Institutes of Health. Mental health will be considered at the session on Saturday

morning under the chairmanship of Dr. Carney. Edward Evarts of the National Institute of Mental Health will speak on the effect of drugs on mental disorders, and I. Arthur Mirsky of the University of Pittsburgh School of Medicine will discuss various related aspects of mental health.

The **National Science Foundation** has recently appointed an **Advisory Panel for Radio Astronomy,** consisting of: M. A. Tuve, Carnegie Institution of Washington, chairman; B. J. Bok, Harvard College Observatory; J. L. Greenstein, California Institute of Technology; J. P. Hagen, Naval Research Laboratory; J. D. Kraus, Ohio State University; R. Minkowski, Mount Wilson and Palomar Observatories; and E. M. Purcell, Harvard University.

The 64th annual meeting of the **Nebraska Academy of Sciences** was held Apr. 23–24, at Omaha, in conjunction with the centennial celebration of the city of Omaha. The host schools were the Creighton University, the University of Nebraska College of Medicine, and the University of Omaha. This year the Chemistry, Physics and Engineering Section was divided and the new Engineering Section was established.

More than 300 were registered and 85 papers were presented in the 7 sections of the Senior Academy. In addition 8 papers were read in the Collegiate Section and 32 papers or demonstrations were given in the Junior Academy. Two papers were presented by members of the University of Nebraska faculty to interest the high school students in careers in science: "New horizons in microbiology" by Carl E. Georgi, professor of bacteriology; "What is there to physics?" by Theodore Jorgensen, Jr., professor of physics. Some 150 high school students registered for the Junior Academy program.

"Fungi and man," the past-presidential address, was presented at the annual banquet by W. W. Ray, chairman of the Department of Botany, University of Nebraska. The evening lecture, "The place of geology in science and life," was given by W. Twenhofel, consulting geologist of Orlando, Fla. Two outstanding symposia were presented: "Paleoecology" in the Earth Science Section, and "Scale of values" in the History and Philosophy of Science Section.

Officers for the coming year are pres., H. M. Cox, Univ. of Nebraska; v. pres., Paul Stageman, Univ. of Omaha; sec., C. B. Schultz, Univ. of Nebraska; corres. sec., Mary Louise Hanson, Univ. of Nebraska; treas., C. E. Rosenquist, Univ. of Nebraska.

The **Summer and Pacific General Meeting of the American Institute of Electrical Engineers** will take place on June 21–25 in Los Angeles, where 250 papers will be presented in 55 sessions. Bradley Cozzens of Los Angeles, general chairman, expects some 2000 participants. Of especial interest to the West Coast will be symposiums on aircraft, computers, atomic energy, mining and metal industry, heat pumps, and power generation.

Elgin B. Robertson, president, will preside and will present the 1953 Lamme Gold Medal to Frank A. Cowan, executive of the American Telephone and Telegraph Co. who is being honored "for his outstanding contributions to long-distance communication and the development of modulating and transmission measuring apparatus of original design and application."

Among the luncheon speakers will be Lee A. DuBridge, president of California Institute of Technology, Lee De Forest, and Walker L. Cisler, president of the Detroit Edison Company.

Miscellaneous

Biographies of some 75,000 scientists will appear in the next revision of ***American Men of Science,*** an increase of about 50 percent over the previous (1949) edition. This is the greatest increase since this biographical directory was founded in 1906. The size of the volume has passed the limits of standard bookbinding machinery, from 3000 to 4500 pages, so that the new (ninth) edition will appear in three parts. Part I, devoted to the physical sciences, will be ready in Nov. 1954. Parts II and III, on the biological and the social sciences will follow.

The Corps of Engineers' Research and Development Laboratories, Fort Belvoir, Va., need several specialists in the field of **electric power generation** to carry on their program of developing improved equipment for the Armed Forces. Applicants must hold a degree in electrical engineering or have considerable practical experience. Salaries range from $3410 to $7040, commensurate with experience. Those interested should apply to Mr. Walter H. Spinks, Chief, Administrative Dept., ERDL, Fort Belvoir.

A. MacRae & Co., Limited, of Bombay, India, published the first issue of the ***Journal of the Indian Medical Profession*** on Apr. 15. In his letter of announcement, N. J. Hamilton, managing director, commented that guest editorials for the new journal would be welcomed.

The **Naval Research Laboratory,** Washington, D.C., has professional vacancies in the physical sciences and in engineering. Inquiries should be addressed to W. G. Torpey, Code 1817, Naval Research Laboratory, Washington 25.

Science in Alaska, 1951, the proceedings of the 2nd Alaskan Science Conference, is now available for $3.00 from Dr. Troy L. Péwé, Secretary, Alaska Division, AAAS, Box 4004, College, Alaska.

The **UNESCO Technical Assistance Program** has announced the following science vacancies: anthropologist, sociologist, ecologist, and hydrologist. Salaries range from $6000 to $8400 a year, tax free. The first three posts are in Brazil, and the last in Mexico. For information address: Technical Assistance Unit, UNESCO, United Nations, New York 17.

Book Reviews

The Permian Reef Complex of the Guadalupe Mountains Region, Texas and New Mexico. A study in paleoecology. Norman D. Newell *et al.* W. H. Freeman, San Francisco, 1953. 236 pp. Illus. + plates. $7.50.

This is a comprehensive and profusely illustrated technical sourcebook on the classic Permian reef complex of West Texas and New Mexico. It emphasizes paleoecologic analysis, with background chapters on regional geologic setting, general stratigraphic features, sedimentary phases, biotal associations, and diagenesis. Its farsighted sponsors and publishers spared no pains to produce a landmark in paleoecology.

The book begins with an excellent summary, which effectively presents the essence of the study. This will encourage many readers through the essential but tedious account of the stratigraphy and on to the more interesting sections that follow. The stratigraphic discussions are hampered by the casual stratigraphic nomenclature and the absence of a clear graphic summation.

The brief chapter on paleontology sticks to biotal distribution. It is supplemented by check lists of fossils in the appendix. The authors postpone critical discussion of problematica, such as *Gymnocodium* and the so-called hydrocorallines (?) as well as the "sycon" sponges.

The chapters on sedimentary phases, diagenesis, and paleoecology are outstanding. That on diagenesis is particularly good, despite some repetition necessitated by the systematic treatment of sedimentary provinces. The treatment of sedimentary phases is second only to this, although of uneven quality. A well-reasoned discussion on pisolites, for instance, contrasts with a rather diffuse section on reef channels. The chapter on paleoecology is lucid and satisfying. Geologists who have followed West Texas Permian stratigraphy will be prepared for many of the conclusions reached, but they will find new interest in the exposition of the stagnant-basin hypothesis, which maintains that the development of organic reefs is encouraged by the marginal upwelling of nutrient-rich waters controlled by a restricted outlet of the Mediterranean type.

A commendable feature of this work is the careful distinction it makes between the organic reef facies proper, the reef complex, and lenticular or otherwise reeflike masses of clastic materials that have nothing to do with organic reefs. These distinctions are important to the oil hunter. Another point of economic interest is the emphasis that the authors place on anaerobic conditions as a prerequisite for the primary accumulation of organic matter in oil-forming quantities. The discussions of fluid migration and silica-calcite replacement are clear and substantial.

Like most books that deal vigorously with current problems, the one under review has not settled all questions of fact and interpretation. A principal conclusion here reached is that aphanitic texture in limestone commonly originates through recrystallization of rocks of originally coarser fabric. Although the evidence is convincing for specific instances considered, the extent to which the interpretation applies remains unsettled. The question of origin of shelf dolomites associated with evaporites is also discussed with inconclusive results, although the authors favor diagenetic alteration from a primary calcium carbonate precipitate. The erroneous record of exclusively algal reefs in the Gilbert Islands (p. 201) should be corrected. Turbidity currents seem overworked in this book as a mechanism for the emplacement of sediments—perhaps because distinction is not consistently maintained between the submarine slide, the turbidity current to which it may lead, and ordinary sediment-bearing currents. Certainly the importance of slumping and density currents in reef-complex sedimentation and erosion deserve emphasis, however, and they have received it here.

The format of the book is good. To be sure, there are some inconsistencies in the bibliography, and some inexplicable omissions in the index. Also Fig. 73 is one-twentieth natural size, not twenty times enlarged. These minor defects, however, are far outweighed by the excellent photographic plates, the many clear and well-executed line drawings, and the large, plain print, so welcome in these times of ultra-economy in publication.

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Fields and Waves in Modern Radio. ed. 2. Simon Ramo and John R. Whinnery. Wiley, New York; Chapman & Hall, London, 1953. 576 pp. Illus. $8.75.

This new edition of an excellent textbook has been enlarged, and extensively revised. Wide use of the original text by the authors and others in courses and in engineering practice has resulted in a number of improvements. These include the use of the mks system of units throughout the text, the inclusion of many more problems and examples, the use of the Smith Chart for transmission line calculations, a new chapter on microwave networks, and some significant additions to the chapters on wave guides and on radiation. Almost every section has been rewritten with the objective of clarifying the presentation. This has been accomplished without loss of the lucid, readable style that was characteristic of the first edition.

The organization of material and method of presentation are essentially unchanged in the new edition. A review of lumped constant networks and transmission lines is followed by a discussion of static fields and the solution of static field problems; then the differential and integral forms of Maxwell's equations are introduced, boundary conditions are discussed, and

the reduction of the field equations to the familiar lumped circuit constants is derived. The remainder of the book is devoted to the problem of the propagation and guidance of electromagnetic waves, including the plane wave analysis in inhomogeneous media, wave guides, resonant cavities, and antennas.

In this textbook, Ramo and Whinnery have succeeded in combining the essential theoretical analysis with the practical viewpoint of engineering applications, so that the reader is led to a clear understanding of the present state of the electromagnetic art. The clarity of exposition and general readability of the text combine with a unity of concept and of presentation to make this an outstanding intermediate level textbook in electromagnetic theory.

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International Review of Cytology, Vol. II. G. H. Bourne and J. F. Danielli, Eds. Academic Press, New York, 1953. 245 pp. Illus. + plates. $11.

Cytology may be looked upon as the common meeting ground of cell morphology, cell physiology, biochemistry, embryology, and genetics—broadly speaking, cell biology. Interpreted in this way, the 14 papers included in the second volume of this annual review can properly belong in such a collection in spite of the wide variety of topics: cytochemistry, electron microscopy, active transport phenomena, growth and differentiation, nucleocytoplasmic relations, integration of enzyme activities, and the physiology of gustatory and olfactory epithelia. Of the 17 contributors eight are American, four English, two Belgian, one Dutch, one Irish, and one German, thus emphasizing the English-American contributions much as the first volume did. The marshaling together of such an assortment of papers is in keeping with the editors' avowed purpose of keeping the "scope as wide as possible" in the "publication of critical discussions of data published elsewhere, and of new theoretical work."

Inevitably the treatment in such a composite group is spotty and uneven. Some of the papers are little more than compendia; others are carefully organized and give critical evaluations and integrations of knowledge in their special areas. No particular orderly sequence of topics is apparent; for example, papers concerned primarily with histochemistry are scattered throughout the volume, interspersed with those dealing with bacteria, electron microscopy, and thermodynamics.

The most extensive review (76 pp. and 356 references), by Hewson Swift, describes and evaluates techniques of chemical analysis at the cellular level, dealing with quantitative aspects of nuclear nucleoproteins. The nature of the Feulgen nucleal reaction is discussed by M. A. Lessler, who concludes that it is the most reliable and specific test for DNA and that quantitative measurements can be made if the sources of error are properly controlled. J. Chayen's paper on ascorbic acid and its cellular localization compares the many methods and postulates the function of vitamin C in cell metabolism. W. L. Doyle's cautious evaluation of methods of microscopic histochemistry for the demonstration of alkaline phosphatase is the shortest paper in the collection (12 pp.; 51 references). Alkaline phosphatases of the nucleus are discussed by Chèvremont and Firket. A penetrating and critical analysis by David Glick of the quantitative approaches currently in use in histo- and cytochemistry overlaps and duplicates to some extent the other papers on histochemistry.

The physiological reviews include Ion Secretion in Plants by Sutcliffe, Multienzyme Sequences in Soluble Extracts, a masterly treatment by Henry Mahler of recent studies on the complex oxidative reactions within the cell, and Conway's treatment of the theory of the redox pump from the thermodynamic standpoint.

The remaining papers cover a wide range of subjects: tissue-culture studies by Gaillard, electron microscopy of tissue sections by Dalton, special cytology of gustatory and olfactory epithelia by Baradi and Bourne, bacterial cytology by Mudd and DeLamater, and grafting and regeneration experiments with *Acetabularia* by Hämmerling.

Included in the volume is a report of a conference of tissue-culture workers held at Cooperstown, N. Y., in 1950. Author and subject indexes are appended. Few typographical arrors are evident and the figures and plates are beautifully reproduced.

The volume should be extremely useful to cell biologists and indispensable to others who, although unable to search out and read all the original papers, require information on current developments in these special areas.

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Causality in Natural Science. Victor F. Lenzen. C. C. Thomas, Springfield, Ill., 1954. 121 pp. $3.

This small volume is a gratifying, unusually sane and complete account of the causality problem in modern science. Written by a philosopher of singular competence in the field of physics, its judgment can always be trusted to be mature in the eyes of scientists as well as philosophers. There is no attempt to present and defend a thesis: different views are impartially offered and discussed. Among the virtues of the book is emphasis upon modern phases of physical science, where causality is reputed to have become of doubtful status or even to have failed. To the reader who has previously been indoctrinated by popular and one-sided accounts, the last chapter, entitled "Causality and quanta," will be particularly helpful and illuminating.

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Lehrbuch der Organischen Chemie. ed. 12. Paul Karrer. Georg Thieme, Stuttgart, 1954. (U.S. distr.: Intercontinental Medical Books, New York). 949 pp. Illus. $14.20.

The burden of maintaining contact with new developments in chemistry is indeed heavy today, considering the large number of advances made in recent years. Thus, the investigator, teacher, and student are indebted to the labors of those who prepare reviews, monographs, textbooks, and the like, making the classification and distribution of chemical knowledge easier.

The volume under review represents the twelfth German edition of a series of organic chemistry textbooks which since 1927 have had wide usage and recognition throughout the scientific world. The renowned author of these classic reference books, Prof. Dr. Paul Karrer, is recognized as well for his many personal contributions to the field of organic chemistry.

In preparing this volume, the author modified his last edition in accordance with recent developments in experimental and theoretical organic chemistry. The new edition, however, is organized basically in the same manner as the previous issue. In the classical tradition the subject material is arranged strictly according to the nature and number of functional groups. In varying degrees, modifications of and additions to all chapters are to be found. As the preface states, it was the author's object to devote more room to organic reaction mechanisms as based on modern theoretical electronic concepts. New material in all phases of organic chemistry is to be found. It is possible to mention here only a few of the new topics that are covered.

The introduction to the text of a great number of reaction mechanisms is noticeable. The free radical and ionic mechanisms for the course of such reactions as isomerizations, halogenations, polymerizations, oxidations, alkylations, carbonyl condensations, acylations, and the like, are included. The author also considers the electronic-theoretical aspects of a variety of subjects, such as oxonium ions, free radicals, resonance states of molecules, ozonides, aliphatic and aromatoc diazo compounds, neighboring group influence, and Walden inversion. Recent advances in the chemistry of actylenes (Reppe syntheses), organometallic reactions, olefins, fluorohydrocarbons, phosphoric acid esters, silicones, and others, are reviewed. A complete section dealing with the chemistry of tropolones is introduced for the first time.

In the field of biological chemistry, the text presents up-to-date material of various metabolic pathways, such as the glucose-ethanol conversion, transamination reactions, peptide synthesis, hexose interconversions, and purine and pyrimidine biosyntheses. The recent developments in the chemistry of a variety of substances of biological importance, such as vitamin B_{12}, coenzyme A, sphingolipids, nucleic acids, folic acid and biotin, are also considered.

Professor Karrer's textbooks are well known for their material dealing with the chemistry of natural products. The new text presents some of the later advances in the steroid, alkaloid, antibiotic, and carotenoid fields. Of great interest is the material on the total synthesis of cholesterol, lycopene, α-carotene, β-carotene, and morphine. The chemistry of cortisone, corticosterone, aureomycin, terramycin, chloromycetin, and mycomycin is included. In the alkaloid field, the recent advances in the chemistry of the senecio, tropanal, curare, morphine, lupine, codeine, colchicine, ergot, and strychnine alkaloids are reviewed.

The use of isotopes in the elucidation of reaction mechanisms is discussed in a section devoted to isotopic organic chemistry.

Tables of miscellaneous information in organic chemistry are omitted from the new edition. The author has extended the section dealing with important dates in the history of organic chemistry to the year 1951.

The quality of the textbook itself is fine. The paper and binding are good. The present German edition will be printed shortly in the English, French, Spanish, and Italian languages. It is the opinion of the reviewer that although designed for the student of organic chemistry, the textbook is an excellent reference source for everyone interested in the field.

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The Challenge of Our Times: Contemporary trends in science and human affairs as seen by twenty professors at the University of Wisconsin. Farrington Daniels and Thomas M. Smith, Eds. Burgess Pub. Co., Minneapolis, 1953. 364 pp. Illus. $3.50.

This book, based on a course, "Contemporary trends in modern civilization," which has been taught at the University of Wisconsin since 1941, consists of 28 chapters, reworked by the 20 lecturers who contributed to the course. It thus represents another of the currently popular attempts to view as an integrated picture a problem that concerns a group of disciplines.

The book is divided into five sections. The first, "Science is everybody's business," contains five chapters that cover briefly: the control of nuclear fission and fusion as examples of scientific developments that profoundly affect society, the history of science, the application of science to modern technology, and the operation of a modern research laboratory. These are followed by two chapters in which the general problems of controlling science in the United States and in Russia, respectively, are treated.

In the second section, "Nations in turmoil," economics, history, genetics, geography, political science, sociology, and anthropology are fused in an eight-chapter view of the changing picture of the control of energy and the problems of agriculture, with diminishing death rates and high birth rates presenting new problems in politics and geography. This section includes chapters on Russia and the Communist way

of life and What is wrong with Communism; other chapters discuss the causes of trouble in Europe and in the world, the emergence of Asia as a trouble spot which has been aroused as Europe became exhausted, and the transition period of the colonial peoples.

The third section is devoted to the world community, with chapters on collective security, the path to peace, the United Nations charter and organization, the possible production of collective security as a halfway step to world government and the problems and rewards when this is attained, and what the consequences of an actual world government would be.

The fourth section contains four chapters dealing, respectively, with what the United States can do in the world picture, the origins of the productive might of the United States, the causes of depressions and inflations, the problems of our foreign policy, and those of United States aid to the world. The final section deals with propaganda and its origins, and the bases for human freedom and happiness.

The authors are experts in their fields, and the individual viewpoints have been well integrated. The general appearance of the book, printed by photo-offset from typed pages, is that of a low-priced textbook in one of its earlier editions. An excellent list of suggested supplementary readings is included, together with short biographical sketches of the authors and a well-prepared index.

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Theory of Equations. Cyrus Colton MacDuffee. Wiley, New York; Chapman & Hall, London, 1954. 120 pp. Illus. $3.75.

This book was written for use as a text in a one-semester course in theory of equations. The mathematical maturity demanded of the student or reader is that of college juniors or seniors. The author intends the book both for those who plan to follow mathematics as a profession and those who will use it as a tool in other fields. He has used modern methods of algebra to present a complete study of linear systems of equations and of polynomials. The introduction of the abstract ideas of rings and fields forms a bridge between elementary algebra and advanced algebra and gives the student an insight into the more advanced work in modern algebra at an early stage in his training. These abstract ideas are introduced so naturally that they do not disturb the basic nature of the course, and a student who is not primarily interested in them will not object to them.

The topics considered include those covered in most of the standard texts on theory of equations, with the one exception that the study of determinants has been omitted. The author thinks that the study of determinants and matrices makes a good course for a second semester's work. The treatment of the topics differs from that of other authors in that the main emphasis is placed upon the theory of polynomials and use is made of modern methods in the development of this theory.

The text begins with a review of the solution of linear equations, and here the idea of a field is introduced. The second chapter contains a concise introduction to the theory of numbers, which some instructors might wish to expand. In the third chapter, the author gives an exact definition of rings and fields. After the definition of polynomials as elements of certain rings, the theory of polynomials is developed rigorously. The text ends with a discussion of Euclidean rings and systems of equations of higher degree.

The computational part of the subject has not been neglected. There are illustrative examples throughout the book. A sufficient number of good exercises (with answers) are provided for student drill.

At first glance, it may seem that there is not sufficient material for a one-semester course. But the abstract ideas of rings and fields cannot be pushed too fast in some classes, and an instructor may find that extra help and drill will need to be provided.

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New Books

Advances in Electronics, Vol. V. L. Marton, Ed. Academic Press, New York, 1953. 420 pp. Illus. $9.50.

Higher Transcendental Functions, Vol. I. Based, in part, on notes left by Harry Bateman; compiled by the staff of the Bateman Manuscript Project, California Institute of Technology. McGraw-Hill, New York–London, 1953. 302 pp. $6.50.

1954 Medical Progress. A review of medical advances during 1953. Morris Fishbein, Ed. Blakiston, New York, 1954. 345 pp. $5.00.

Human Behavior in the Concentration Camp. Elie A. Cohen. Trans. by M. H. Braaksma. Norton, New York, 1953. 295 pp. $5.00.

Infrared Absorption Spectra of Steroids: An Atlas. Konrad Dobriner, E. R. Katzenellenbogen, and R. Norman Jones. Interscience, New York, 1953. Introduction + 308 spectra charts. $11.50.

Sound. A physical textbook. 5th rev. ed. E. G. Richardson. St Martin's Press, New York; Edward Arnold, London, 1953. 352 pp. Illus. $5.00.

Introduction to Aeronautical Dynamics. Manfred Rauscher. Wiley, New York; Chapman & Hall, London, 1953. 664 pp. Illus. $12.00.

Who's Who in British Science, 1953. British Book Centre, New York, 1954. 292 pp. $9.00.

Evolution: Die Geschichte ihrer probleme und Erkenntnisse. Walter Zimmerman. Verlag Karl Alber, Freiburg–München, Germany, 1953. 623 pp. Illus. + plates. DM 32.

Main Currents of Scientific Thought. A history of the sciences. S. F. Mason. Abelard Schuman, New York, 1954. 520 pp. $5.00.

Man, Rockets and Space. Burr W. Leyson. Dutton, New York, 1954. 188 pp. Illus. $3.50.

Music Therapy. Edward Podolsky, Ed. Philosophical Library, New York, 1954. 335 pp. Illus. $6.00.

Technical Papers

The Physiologic Closure of the Ductus Arteriosus in Newborn Infants: A Preliminary Report*

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The exact time of functional closure of the ductus arteriosus in the normal human infant has never been determined. Studies on anatomical specimens have shown that complete morphologic closure requires from 6 to 8 wk (*1, 2*). It is fairly well agreed, however, that the ductus arteriosus is closed to the passage of significant quantities of blood long before this occurs. Using the technique of angiocardiography, Barclay and his coworkers (*3, 4*) and Barcroft (*5*) have suggested that physiologic closure in lambs may occur within a few minutes after birth. More recent animal experiments have disputed this fact (*6*), and one study using dogs and a radioactive isotope tracer method has shown a gradual closure of the ductus over a period of days (*7*). Some authors have questioned the applicability of experiments in animals to human infants (*8*).

The present study was stimulated by the observation that newborn infants occasionally show definite cyanosis of the lower part of the body but not of the upper portion. Regional cyanosis of this variety is occasionally observed in adults and older children who have a patent ductus arteriosus with pulmonary hypertension and a right-to-left shunt through the ductus (*9, 10*); and since the infant has a physiologic right ventricular hypertrophy suggesting a high pulmonary pressure, it was felt that this cyanosis of the lower extremities occasionally seen in the newborn might be due to a flow of blood in the fetal direction through an open ductus.

To investigate this possibility, 14 studies were done on 12 normal newborn infants at varying times after birth. Arterialized capillary blood from the right hand and from the foot was obtained with minimal exposure to air by a previously described method (*11*), and the oxygen contents and capacities were determined by the microtechnique of Roughton and Scholander (*12*). The right hand was selected rather than the left because of the proximity of the left subclavian artery to the ductus and the observation that occasionally the left upper extremity will show arterial unsaturation in the presence of a veno-arterial shunt through the ductus (*13*).

In all of the infants, the blood samples from the right hand showed an oxygen saturation of more than 90 percent, indicating that true arterial blood was obtained. Of the 14 studies, 8 showed an oxygen saturation in the foot that was significantly lower than that of the right hand. Since the error of the method is approximately ± 2.5 in terms of percentage of saturation, differences falling within this limit are not considered significant. These differences in oxygen saturation between the right hand and the foot are shown in Table 1.

Table 1. Differences in oxygen saturations of the right hand and the foot.

Infant	Age-hours	Oxygen saturation of right hand (%)	Oxygen saturation of foot (%)	Percentage difference in saturation between hand and foot + Foot saturation higher − Foot saturation lower
Cl.	1	94.4	90.4	− 4.0
Ma.	1½	93.4	84.4	− 9.0
Be.	1½	92.2	83.4	− 8.8
Al.	2	93.7	82.7	− 11.0
De.	2½	91.4	87.3	− 4.1
La.	11	91.3	91.5	+ 0.2
Sm.	20	97.2	90.7	− 6.5
Fr.	27	90.5	82.5	− 8.0
Mo.	42	94.3	92.0	− 2.5
Al.	46	94.0	79.5	− 14.5
Mi.	81	90.0	87.3	− 2.7
Cr.	94	93.0	94.3	+ 1.3
St.	108	93.6	92.6	− 1.0
Al.	118	91.7	91.3	− 0.4

In all of the five infants studied, 1 to 3 hr after birth, the oxygen saturation of the blood from the foot was significantly lower than that from the hand, indicating the presence of a veno-arterial shunt to the lower part of the body. Three of the five infants studied, 3 to 72 hr after birth, showed a saturation in the foot significantly lower than that of the right hand. None of the four infants more than 3 days old showed a significant difference in saturation between hand and foot.

One infant (Al., Table 1) showed a marked difference in oxygen saturation between hand and foot 2 hr after birth, a similar difference at 2 days, and no difference at 5 days, indicating disappearance of the veno-arterial shunt.

These findings indicate that the ductus arteriosus is patent and that it is the site of a veno-arterial shunt of the fetal type in most newborn infants during the first 3 hr of life. This situation persists in a significant

* This study was aided in part by a grant from the San Francisco Heart Association.

number of infants up to the age of 3 days. In the infants of this age who no longer demonstrate a shunt, either functional closure of the ductus arteriosus has occurred or, owing to a decrease in pulmonary vascular resistance, flow through the ductus has changed from the fetal to the adult direction. In most infants more than 3 days old, the ductus is either closed to the passage of blood or a change in direction of flow has occurred.

Further studies are being carried out in this laboratory to determine more accurately the incidence of this phenomenon and to study the factors that affect alterations of flow through the ductus.

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Evidence for a Diurnal Pulse in Stream Phytoplankton

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Since the discovery of stream plankton (potamoplankton) about 1890, an extensive literature has accumulated, which includes a number of merely qualitative lists of species from various rivers, many quantitative reports of phyto- and zooplankton, numerous 12-mo studies listing either qualitatively or quantitatively the species present in stream plankton, and a relatively small amount of experimental work. Much of this literature is reviewed by Des Cilleuls (*1*).

In small streams lacking impoundments, it appears that nearly all the organisms carried as plankters originate from the benthos as attached forms or, in many cases, as single cells or filaments mixed with the upper layer of sediments that settle in quiet areas. Steuer (*2*) lists eight environmental factors that regulate the potamoplankton both qualitatively and quantitatively, but no mention is made of the diurnal factor. It would seem that later authors would almost certainly have taken up this subject; however, a diligent search has yielded no reference to work dealing with diurnal changes in stream plankton.

During 1952 and much of 1953, the algae of the Saline River in southeastern Michigan were under close observation. The Saline is a small stream located in Washtenaw County about 7 mi south of Ann Arbor that is polluted by both domestic and industrial wastes. In the summer of both these years, this stream exhibited in its polluted portion a region about 4 km in length that was dominated by the benthic diatom *Nitzschia palea* (Kütz.) W. Smith growing in a conspicuous brown sheet or layer on submerged rocks or silt deposits. Filamentous algae were abundant at certain seasons, but at the time and place of the work here reported they did not represent a significant element of the plankton or an important vehicle for the transport of entrapped or epiphytic organisms.

A very dense net plankton composed almost entirely of *N. palea* can be collected from this stream in the summer months but only in and immediately below the course of the river within which *N. palea* is abundant as a bottom organism. The *Nitzschia* plankton is, therefore, obviously of benthic derivation. This appeared to be a favorable situation in which to find a diurnal variation in stream plankton, if indeed such a variation existed anywhere. Two locations were accordingly chosen, one near the middle (Saline Mills) and one near the downstream end of this 4-km portion, for making comparative observations at different hours of the day. At each point, the net plankton was sampled at dawn and in late afternoon of Aug. 13, 1953. Counts of this material showed that planktonic *N. palea* was much more abundant at both stations in the afternoon than at dawn.

In an effort to demonstrate a diurnal periodicity more clearly, plankton samples were then taken at approximately hourly intervals throughout a 24-hr period on Aug. 25 and 26, 1953, at the Maple Road station, which is about 5 km below the industrial and domestic sewage outfalls. Throughout the sampling period, the weather remained clear and cloudless. Fair or cloudless weather, favorable for algal growth, had furthermore prevailed for at least 2 wk prior to the sampling period. Water level remained approximately the same throughout this period, with a variation of ±1.5 mm recorded. Water temperatures varied between 17.8 (6:15 A.M., Aug. 25) and 24.0°C (4:10 P.M., Aug. 25), air temperatures between 15.0 (6:15 and 7:15 A.M., Aug. 25) and 31.7°C (2:10 and 3:10 P.M., Aug. 25). I estimate that at this time (Aug. 25–26) it required about 5.8 hr for water in midstream, at a surface speed of 1.9 m/sec, to pass from the upper reaches of the *Nitzschia* community to the sampling point at Maple Road.

All samples were surface water taken from exactly the same point in the stream. Plankton was collected, and 20-field counts made, with minor variations, according to the method of Verduin (*3*). Because of the difficulty of distinguishing dead cells from certain moribund cells, all diatoms both dead and living at the time of collection were counted. Few of the frustules were completely empty, although cells obviously dead made up a larger percentage of the total during

Table 1. Hourly totals for plankton organisms in the Saline River, 1953.

Time	*Nitzschia palea* (10^3 units/liter)	All other phytoplankters (10^6 units/liter)
Aug. 25		
5:15 A.M.	66	10.7
6:15	103	12
7:15	112	8.9
8:15	114	7.5
9:15	102	2.7
10:10	299	8.5
11:05	2290	14.7
12:05 P.M.	1340	9.8
1:20	880	11.1
2:15	1460	18.3
3:10	807	21
4:10	389	8.5
5:15	382	7.1
6:05	238	11.6
7:40	153	14
8:30	239	13
9:25	260	15.2
10:15	168	8.9
11:15	207	12.5
Aug. 26		
12:15 A.M.	116	7.1
1:15	184	18.3
2:15	139	8.5
3:15	150	7.6
4:20	121	6.2

the nocturnal hours than during the day. It should be noted that single empty valves are given equal importance with complete cells in this type of count.

The results are shown in Table 1. It is clear that *N. palea* entered the plankton in quantity in late morning. Its numbers fell off sharply in midafternoon, and during late afternoon and evening a slow return to the nocturnal minimum took place. The principal nonphotosynthetic organism in the plankton consisted of bacterial filaments, apparently fragments of *Sphaerotilus natans* Kütz. Other chlorophyll-bearing plankters included *Nitzschia linearis* W. Smith, *Navicula cuspidata* Kütz., *Dinobryon sertularia* Ehrenb., and fragments of *Stigeoclonium tenue* Kütz. None of these exhibited any clear tendency to be more abundant in the plankton at one time of day than at another.

As factors in the diurnal periodicity exhibited by *Nitzschia palea*, both water temperature and water level can very likely be ruled out, since neither varied significantly in such a way that its variations could be correlated with changes in the phytoplankton.

Save for dissolved gases, the results of chemical analyses of the river water for various organic and inorganic components made over a period of 14 mo gave no reason to suppose that there is either a consistent change from hour to hour or any consistent diurnal variation, although such a variation was not specifically looked for. The region dominated by benthic *N. palea* is first evident about 0.8 km below the two principal polluting outfalls. There is no apparent periodic variation from hour to hour or from day to day in the amount of waste delivered from either of these outfalls. Near the point where the industrial outfall enters the stream, it has been the practice each evening to dump into the stream several gallons of dilute sulfuric acid largely neutralized by alkali. However, the stream is high in bicarbonate and well buffered. During the 12 mo in which *p*H determinations were made on 126 water samples from points 0.1 to 5.0 km below these outfalls, the *p*H showed little variability—the extremes were 7.60 and 8.55. It seems clear that the dumping of acid in itself has little effect on the aquatic environment at more than a few dozen meters below the outfall. From the standpoint of time, furthermore, the acid waste appears to be eliminated as a causative factor in the midday *Nitzschia* pulse, for the latter reached its peak after 10 A.M., at a time when the dissipated acid would already be found several kilometers below the sampling station.

Earlier workers, including Butcher (*4*) and Jónasson (*5*) have observed the detachment and rise of filamentous benthic algae from stream bottoms. A similar phenomenon, starting in late morning on fair summer days and continuing until midafternoon, has been observed several times during my work on the Saline River. This phenomenon is caused, at least in part, by the production of oxygen bubbles in photosynthesis as a result of the much greater available light during the midday hours. The buoyancy of the algal mass is then greatly increased; it rises to the surface and moves slowly downstream, constantly shedding filaments or cells, which become part of the potamoplankton. It is probable that this midday production of oxygen is the mechanism for the entry of *Nitzschia palea* into the plankton as here recorded, although most of the *Nitzschia* cells rising into the current apparently did so independently of their neighbors. Floating or suspended masses of cells were seldom seen.

To the stream ecologist, the diurnal pulse thus observed is significant because of the increasing pollution of many small rivers and the consequent probability that other streams whose plankton has been or will be studied exhibit similar regions dominated by photosynthetic unicells that are benthic but unattached. For the area immediately downstream from such a benthic community, a plankton sample taken once, at an indiscriminate hour of the day, as has been commonly done in the past, must hence be regarded as untrustworthy.

The phenomenon here recorded may be limited geographically to small, and perhaps to polluted, streams. The magnitude of the diurnal variation is probably dependent upon any factor that might limit the entrance of benthic organisms into the plankton or otherwise influence their representation there. Plankton samples taken on cloudy days, or at some point

other than the downstream end of a region dominated by benthic unicells, or in periods of rapidly changing water level, or even from a stream receiving similar pollutants but larger in volume of flow might be expected to show much less marked periodicity.

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Distribution and Heredity of Blood Factor U

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In a previous report (*1*), a new blood factor **U** was described, sensitization to which caused a fatal hemolytic transfusion reaction (*2–4*). The purpose of the present report is to describe further observations on the distribution and heredity of this blood factor.

Tests for factor **U** were carried out on blood specimens from 1100 Caucasoids and 989 Negroids. As is shown in Table 1, all 1100 Caucasoids had the blood factor **U**, and only 12 of the Negroids lacked the factor. The A-B-O groups, M-N-S types, Rh-Hr types, and Kell types of these 12 individuals, as well as the patient who had the hemolytic reaction and from whom the antiserum was obtained, are shown in Table 2. From these results, factor **U** apparently bears no relationship to any of these blood group systems, except possibly the M-N system. Moreover, the distribution of the **U** factor precludes any relationship to Duffy, Kidd, Lutheran, or Lewis systems.

The peculiar racial distribution suggested the possibility that factor **U** might be an alternate of the Hunter factor (*4*) or Henshaw factor (*5*). As will be shown later, the low frequency (2.7 percent) of the Henshaw factor found by Chalmers, *et al.* (*6*) among Negroids would tend to exclude that possibility, but the results obtained by them for the Hunter factor (21.7 percent) closely approximate the expected value. However, tests for these factors kindly carried out by William S. Pollitzer, Research Fellow, Institute of Human Variation, Columbia University, on a blood specimen from an individual of type uu were negative for the factors Henshaw and Hunter. This was contrary to expectations were either of the latter an alternate of **U**.

With regard to the heredity of the blood factor **U**, the simplest and most plausible theory is that factor

TABLE 1. Distribution of the blood factor **U**.

Racial group	Number of individuals		
	Positive	Negative	Total
Caucasoids	1100	0	1100
Negroids	977	12	989

TABLE 2. Blood types of individuals with blood lacking factor **U** (type uu).

Blood of	A-B-O group†	M-N-S type	Rh-Hr type	Kell type
Patient 1*	B	MN	$\mathfrak{R}h_1rh$	kk
2	O	N	Rh_1rh	kk
3	B	N	Rh_o	kk
4	O	MN.ss	$\mathfrak{R}h_o$	kk
5	B	N	Rh_o	kk
6	O	MN.ss	Rh_o	kk
7	B	MN.ss	Rh_o	kk
8	O	MN.ss	Rh_1rh	kk
9	O	MN.ss	rh	
10	O	N.ss	Rh_o	
11	O	MN.ss	Rh_2	
12	B	N	Rh_1rh	kk

* The numbers 1–12 represent the 12 individuals referred to in Table 1.
† Only individuals of group B and group O were tested, because the patient's serum contained anti-A agglutinins.

TABLE 3. Family studies on blood factor **U**.

Family number	Father	Mother	Children		
1		O N Rh_1rh kk† uu	O N rh'rh kk ♀ U		
2	O MN.ss $\mathfrak{R}h_o$ kk† uu	O N.ss Rh_1rh kk U	O N.ss Rh_o kk ♀ uu	O N.ss Rh_o kk ♀ uu	O N.ss $\mathfrak{R}h_o$ kk ♀ U
3			B MN.ss Rh_o ♂† uu	O M Rh_o kk ♂ U	
4	O MN.ss rh† uu	O MN.S Rh_1rh kk U	O MN.ss Rh_1rh kk ♀ U	O MN.ss Rh_1rh kk ♂ U	

† Propositus.

U, like other blood factors, is inherited as a simple Mendelian dominant. An attempt was made to study relatives of the rare individuals of type uu, in order to verify this hypothesis. As is shown in Table 3, we were able to examine two complete families, and in two other cases we tested the daughter and brother of the propositus. In families 1, 3, and 4 of Table 3, the other members of the family all proved to belong to type U. In family 2, the wife belonged to type U, but two of the three children belonged to type uu. The occurrence of two additional individuals of the rare type uu in such a short series of families confirms the hereditary nature of this blood factor. Presumably, the factor is inherited by a pair of allelic genes U and u, where gene U determines the presence of the factor and gene u its absence. Thus, type uu individuals are always homozygous (genotype uu), while type U individuals may be homozygous (genotype UU) or heterozygous (genotype Uu). The fact that in family 4, both children belong to type U indicates that gene U is dominant to gene u. In family 2, the type U parent is evidently heterozygous, accounting for the occurrence of type uu in the children.

From the distribution of the types, the gene frequencies are readily calculated. In Caucasoids, gene u is apparently absent, or at least very rare. Since the frequency of type uu in Negroids is 1.21 percent, the frequency of gene $u = \sqrt{\text{type uu}} = \sqrt{0.0121} = 11$ percent. Therefore, the frequency of gene $U = 89$ percent.

From these values, the frequencies of the three genotypes among Negroids can be calculated as follows:

genotype $UU = (U)^2 = 79.2$ percent,
genotype $Uu = 2(U)(u) = 19.6$ percent,
genotype $uu = (u)^2 = 1.2$ percent.

Thus, approximately one-fifth of type U individuals among Negroids are heterozygous, and it is not surprising that we encountered such a family in our short genetic study. Moreover, if there is a blood factor u corresponding to gene u, the expected frequency of the factor in Negroids would be 20.8 percent. As has already been pointed out, the results obtained by Chalmers, *et al.*, for the Hunter factor (21.7 percent) are remarkably close to this value. Moreover, the fact that all the type uu individuals found to date belong to type N or type MN also suggests a relationship to the Hunter factor, since one of us had previously found (*7*) that blood specimens containing the Hunter factor belonged to type N or type MN. However, as has already been pointed out, the fact that a type uu blood failed to react with anti-Hu serum is evidence that Hunter is not an alternate of U.

Since factor U proves to be important for the selection of donors for transfusion to Negroids, a source of specific antiserum is desirable. We had available numerous immune rabbit serums prepared by injections of human blood in order to produce anti-M and anti-N serums. Since all the rabbits had almost certainly received blood of type U, the possibility existed that the antiserum might have U antibodies. Accordingly, 11 different serums were absorbed with type uu blood in order to remove the human species-specific antibodies. Tests after absorption failed to reveal the presence of any U antibodies, however. Experiments are now in progress in which one of the type uu individuals is being immunized by injections of type U blood in order to produce typing serum.

Note added in proof: After four monthly injections, there is still no evidence of specific antibody formation.

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Effect of Synthetic Thioctic or Alpha Lipoic Acid on the Voluntary Alcohol Intake of Rats

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It has been shown that a proportion of rats fed a diet containing only 11 pure vitamins as a source of the vitamin-B complex increase their voluntary alcohol intake, and that a large proportion of these rats decrease their intake when they receive a supplement of liver or yeast (*1*). The substance present in liver and yeast responsible for this effect has been called factor N_1 (*2*).

On the other hand, it has been shown that some microorganisms utilize pyruvate only when the medium contains a factor that has been isolated and synthetized and given the names of thioctic acid (*3*) and alpha lipoic acid (*4, 5*).

Since we have assumed, as a working hypothesis, that the increased voluntary alcohol intake observed in the aforementioned experimental conditions could be the consequence of a slight disturbance in the carbohydrate metabolism at a step higher than the C_2 compounds, it seems desirable to study the effect of this synthetic substance on the voluntary alcohol intake of rats depleted of factor N_1 (*6*).

The alpha lipoic or thioctic acid was given to each experimental rat during a period of 4 to 10 days, after at least 90 days of feeding the aforementioned diet and after voluntary alcohol intake was sufficiently stabilized. The alcohol intake was measured daily, and the average for the 11th to 20th days after the first

dose of thioctic acid or alpha lipoic acid was compared with that of the 10 days preceding the supplement.

There is a proportion of rats in our colony that do not show a decrease of the alcohol intake after liver supplement. Unfortunately, we cannot select them before starting the experiment. For this reason, we have to separate them afterward, testing the effectiveness of liver in each of the experimental rats. For this purpose, the rats received dry liver in doses of 2 g per 100 g body weight per day during 10 days, and the alcohol intake of this new period was also measured. Obviously, we considered in this study only the results obtained in the rats that decrease their alcohol intake after liver supplement.

factor N_1 exhibit a slight decrease of the alcohol intake when the diet is supplemented with alpha lipoic or thioctic acid, and that this decrease is significant around the 2-percent level. On the other hand, they show that liver supplement induced a more consistent decrease of the alcohol intake of the same rats.

Since the activity of dry liver is equivalent to 2 to 4 μg per gram (*7–9*), the liver supplement (total dose 20 g per 100 g body weight) represents 40 to 80 μg of thioctic or alpha lipoic acid. Thus, it is clear that there are rats sensitive to liver and nonsensitive to equivalent or higher doses of alpha lipoic or thioctic acid; hence, the effect of liver can be attributed only in part to the thioctic or alpha lipoic acid contained in it. If we consider as factor N_1 any nutrient, differ-

Table 1. Effect of alpha lipoic or thioctic acid and of liver on the voluntary alcohol intake (milliliters per 100 g body weight per day) of N_1-depleted rats.

	Line	Range		Arithmetic mean	Standard deviation	t*
		Lower	Higher			
Experimental: 31 rats (17 males and 14 females)						
10 days before supplement (*A*)	1	0.28	1.02	0.56 ± 0.031	0.17 ± 0.022	
11th to 20th days after first dose of alpha lipoic or thioctic acid supplement (*B*)	2	.12	0.71	.46 ± .026	.14 ± .018	(1) 2.4
10 days on liver supplement (*C*)	3	.02	.49	.20 ± .025	.11 ± .017	(1) 7.0
A–B	4	−0.21	.41	.11 ± .026	.14 ± .018	
B–C	5	−0.08	.51	.26 ± .020	.15 ± .020	(4) 3.8
Control: 33 rats (15 males and 18 females)						
Same days as *A*	6	0.25	.72	.41 ± .022	.12 ± .016	
Same days as *B*	7	.07	.75	.40 ± .038	.22 ± .027	
Same days as *C*	8	.14	.81	.40 ± .033	.19 ± .023	
A–B	9	−0.29	.55	.01 ± .033	.19 ± .024	(4) 2.4
B–C	10	−0.19	.23	.00 ± .019	.11 ± .013	(5) 7.6

* The figure in parentheses represents the line with which the comparison was made.

On the other hand, sometimes spontaneous fluctuations of alcohol intake occurs in rats. This made it necessary to use a control group composed of rats depleted of factor N_1 and sensitive to liver supplement. The control group did not receive any supplement during the days that the experimental groups were studied.

The experimental rats were divided into four groups of 10 rats each, receiving alpha lipoic or thioctic acid orally in total doses of 62.5, 125, and 750 μg per 100 g body weight, and subcutaneously 62.5 μg per 100 g body weight. Of these 40 rats, only 31 (17 males and 14 females) were sensitive to liver. Since the results did not differ among the groups, all of them were considered as a whole in the statistical analysis. The control group included 33 rats (15 males and 18 females).

Table 1 summarizes the results obtained in the experimental rats and in the controls.

The experimental data show that rats depleted on

ent from the B vitamins known before the discovery of alpha lipoic or thioctic acid, that induces a decrease on the voluntary alcohol intake of deprived rats, we have to conclude that this factor is not a single substance but is composed, at least, of alpha lipoic or thioctic acid and of another substance yet unknown.

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Communications

Trilobite Protaspids Showing Superfamily Differences

Fundamental differences of suprageneric nature are indicated in the structure of immature forms of the trilobites *Olenellus gilberti* Meek and *Antagmus* sp. from beds of Early Cambrian age and *Poliella denticulata* Rasetti from beds of early Middle Cambrian age in the Pioche district of Nevada. The three species are among the oldest known representatives, respectively, of the superfamilies Olenelloidae, Ptychoparioidae, and Corynexochoidae.

The structural differences of the immature forms are shown principally in the development of the glabella. In *Antagmus* sp. the glabella passes through three phases before reaching a condition comparable to that of the adult. In the youngest phase, the protaspid, the glabella is roughly T-shaped and it reaches to the anterior margin of the cephalon. The T-shape results from the nondifferentiation of the ocular lobe from the anterior part of the glabella. In the second phase, the earliest meraspid degrees, dorsal furrows outlining the anterior part of the glabella differentiate the glabella from the ocular lobes, but the glabella continues to extend to the anterior margin of the cephalon. In the third phase, later meraspid degrees, the frontal area appears and the glabella becomes progressively shorter until it reaches the adult condition. Similar developmental sequences are shown by Störmer [*Norsk Geol. Tidsskr.* **21**, pl. 1 (1942)] for *Blainia*(?) and *Olenus*.

In the protaspid of *Poliella denticulata* Rasetti the anterior portion of the glabella is already differentiated from the ocular lobes, comparable to phase two of the glabellar development of *Antagmus* sp.

In the protaspid of *O. gilberti* Meek the glabella and ocular lobes are differentiated and the frontal area is developed to a degree comparable to phase three of the glabellar development of *Antagmus* sp. The protaspid of *O. gilberti* Meek is therefore much more like the adult than the protaspids of *P. denticulata* Rasetti and *Antagmus* sp. Similar protaspids are illustrated by Störmer (*op. cit.*) for species of the olenellid genera *Elliptocephala* and *Paedumias*.

These observations indicate that there are recognizable differences among even the smallest fossilized remains of some of the earliest representatives of three groups of trilobites considered by most authors as superfamilies, and that these differences are shared by other trilobites placed in those superfamilies. The study of trilobite protaspids may be of fundamental importance to any future considerations of the basic principles of trilobite classification.

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Sclerotia in an Operculate Discomycete

True sclerotia have apparently never been reported in an operculate discomycete. Members of the genus *Wynnea*, however, produce an anomalous structure termed a sclerotium by some authors (*1, 2*). One of us (*3*) has referred to the structure in *Wynnea* as a "sclerotium," recognizing that it differs fundamentally from a true sclerotium in its internal structure. Recently the development of true sclerotia in an apparently undescribed species of *Pyronema* has been observed and is reported in this note.

Sclerotia, but no apothecia, were observed to develop on a coconut-milk medium supplemented with essential mineral elements and on a synthetic medium, Czapek's I (*4*). The latter medium has consistently yielded sclerotia in liquid and in 1.5 percent agar cultures. The sclerotia are spherical to irregular in shape, generally no larger than 1 mm in any dimension, and occur scattered over the surface of the medium. In cross section, the sclerotia are characterized by an outer rind of compacted, distorted, dark-colored cells and an inner, almost colorless medulla of thinner walled, less compacted pseudoparenchyma. The sclerotial anatomy is strikingly reminiscent of the kind found in certain members of the Sclerotiniaceae, a family of inoperculate discomycetes.

After surface sterilization of the sclerotia and transfer of them to sterile water agar (1.5 percent), mature apothecia, typical of the original *Pyronema* isolates, were produced. Single ascospores from these apothecia were transferred to the type of medium favoring sclerotial formation, and typical sclerotia were again produced. The fungus has been carried through a number of generations, from ascospores to sclerotia and back to ascospores, by repeating the foregoing techniques.

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Recent Progress in the Study of Pacific Coast Paleozoic Faunas

Exceptional advances in the study of Paleozoic rocks and fossils of the Far West have been made since 1943. From southern California to Oregon, detailed geologic mapping reveals new paleontologic data germane to a better understanding of Pacific Coast Paleozoic history.

Paleozoic rocks occupy great areas of California and Oregon in (i) the Mojave Desert, (ii) the Death Valley-Inyo region, (iii) the Sierra Nevada Mountains, (iv) the Klamath Mountains, and (v) the Upper Crooked River region of Oregon. In the Colorado Desert, Peninsular Ranges, Tehachapi Mountains, and the Coast Ranges, certain undated metamorphic rocks are also very probably Paleozoic age in part.

South of the great Garlock fault the pre-Tertiary rocks of the Mojave Desert and northern San Bernardino Mountains are prevailingly metamorphic and granitoid. This broad region embraces scattered areas of mildly altered or unaltered Paleozoic rocks bearing fossils of Cambrian, Carboniferous, and Permian ages. Within the Mojave region, however, Ordovician and Silurian rocks are yet unrecognized, and rocks of Devonian age occur only near the eastern margin.

Since 1943 the broad Death Valley-Inyo region, north of the Garlock fault, has yielded important additions to the Cordilleran Paleozoic faunas. With thickness of the order of 23,000 ft, the Paleozoic column here seemingly shows few major gaps between Lower Cambrian and upper Permian. Of particular interest are newly recognized faunas from Upper Ordovician, Silurian, Lower Devonian, Lower Mississippian, Pennsylvanian, and Permian rocks.

Studies of fusulinids from zoned Pennsylvanian and Permian sections in the Inyo Range have proved of local value in structural interpretation and may have broad stratigraphic application in the Great Basin, Sierran, and northern California regions. In general it may be said that the Death Valley-Inyo Paleozoic faunas indicate relationship to the central Great Basin column.

Comprehensive study of the very important Cambrian section in the northern Inyo Mountains (Waucoba area) has thus far not been carried to fruition. Interest in such undertaking, however, is now growing.

Mapping by U.S. Geological Survey parties in the Sierra Nevada belt, with emphasis upon search for mineral deposits, has recently brought to light new Paleozoic fossil occurrences of great interest. The newly discovered faunas are of Ordovician, Carboniferous, and Permian ages. Except for the Silurian strata long ago found at Taylorsville, Calif., the existence of middle Paleozoic strata in the Sierran belt is still in doubt. It is also not yet known with assurance whether the Sierran Paleozoic rocks bear closest faunal relationship to the Great Basin province or to the Klamath Mountains region.

In the Klamath Mountains of northern California, significant additions to Silurian, Devonian, Carboniferous, and Permian faunas have recently been made. Paleontologic investigations now in progress in the Redding district of northern California confirm the Devonian age of certain limestones and punky shales assigned to the Kennett formation. However, the relations of most faunas of the Kennett formation, particularly the coral assemblages originally assigned to Middle Devonian, still remain obscure.

The Mississippian units (Baird shale) of the Redding area carry the brachiopod *Gigantoproductus*; they correlate with the *Gigantoproductus-Striatifera* fauna of Old World affinities as found in the Coffee Creek formation of Oregon [C. W. Merriam and S. A. Berthiaume, *Geol. Soc. Amer. Bull.* **51**, 1935 (1940)]. Comparison of coral and fusulinid assemblages from the Permian (?) McCloud limestone and the Nosoni formation of Permian age at Redding with those of the eastern Oregon, Sierran, and Death Valley-Inyo areas, may also be expected to yield data of paleogeographic interest.

Fossil faunas now under investigation from several localities in the northern Klamath Mountains provide evidence of widespread and varied Silurian deposition in this portion of the Pacific Coastal belt. No direct relationship to known Silurian faunas of the Great Basin is so far indicated by provisional studies of the Klamath Silurian rocks.

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New High-Pressure Phases of Silica

L. Coes [*Science* **118**, 131 (1953)] has described a new high-pressure crystalline phase of silica, produced at 35,000 atm and 500 to 800°C. Paul P. Keat, graduate student in the School of Ceramics at Rutgers University, has recently discovered another crystalline phase of silica, produced hydrothermally above the critical point of water, under certain conditions of chemical environment. Information on this phase will probably be published within the next few months.

Each of the new phases of silica has a distinctive structure, making it quite different from the well-known crystalline phases, quartz, tridymite, and cristobalite.

Fearing that the discoverers might be too modest to name the new phases after themselves, I have sought and obtained permission from Coes and Keat, both of whom are now at the Research Laboratories of the Norton Company in Worcester, Mass., to propose names for the new phases—namely, *coesite* for the phase produced at 35,000 atm, and *keatite* for the phase produced hydrothermally. W. T. Schaller, of the U.S. Geological Survey, has been kind enough to check his collection of lists of new mineral names and tells me that these two names have not been previously used for any mineral.

Schaller took occasion to register his objection to the use of the suffix *-ite* on the ground that it is an established custom to give this termination only to names of natural minerals. Without attempting to pass on the merits of this principle, I would only remark that it is very convenient to have a single word by which to refer to a new substance or a new phase of an old substance, and that metallurgists and chemists have long been accustomed to name products after the discoverer or some other individual by the use of the termination *-ite*. I need only refer to austenite and

carnegieite. On the other hand, no writer is justified in completely ignoring a convention that is already well established, as the industrial chemists have done in naming their petroleum derivatives "petrochemical," when, as nearly everybody knows, petrochemistry is the chemistry of rocks.

As an alternative for the benefit of any reader who wishes to stand firmly on the mineralogist's principle, I suggest that he call Coes' new phase of silica *silica C* and that he call Keat's phase *silica K*.

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Tavorite and Barbosalite: Two New Phosphate Minerals from Minas Gerais, Brazil

Two more new phosphate minerals—tavorite and barbosalite—have been discovered in the Sapucaia pegmatite mine in Minas Gerais, Brazil. Three other minerals, recently described in the mineralogical literature, were named frondelite, faheyite, and moraesite. The Sapucain permatite is granitic in composition, is confocally zoned on the basis of texture and mineral composition, and has had a significant production of muscovite and beryl.

Tavorite and barbosalite are intimately intergrown secondary phosphate minerals that occur with many other phosphate minerals in the pegmatite: heterosite, ferrosicklerite, hureaulite, vivianite, strengite, metastrengite, childrenite, variscite, frondelite, faheyite, moraesite, triphylite, montebrasite, and apatite. Other accessory minerals include spodumene, beryl, tourmaline, and sulfides. Quartz, perthite, albite, and muscovite are the essential minerals of the rock.

Tavorite is a hydrous lithium ferric phosphate, the ferric analog of montebrasite with which it is isostructural. It is named in honor of Elysiario Tavora, professor of mineralogy, Universidade do Brasil, Rio de Janeiro. The mineral occurs as a yellow very fine grained aggregate with a mean index of refraction of 1.807 and a specific gravity of 3.29. The chemical analysis shows the following percentages: Li_2O 7.64, FeO 2.39, MnO 1.47, Fe_2O_3 42.57, P_2O_5 39.78, H_2O^+ 5.76, and H_2O^- 0.40. The formula, as derived from the chemical analysis, is

$$(Li_{0.90},Fe^{II}_{0.06},Mn^{II}_{0.04})Fe^{III}_{0.94}(PO_4)_{0.99}(OH)_{1.13}$$

as compared with the ideal formula $LiFe(PO_4)(OH)$. X-ray powder data show principal *d*-spacings at 3.045, 3.285, 4.99, 4.68, and 2.474 A.

Barbosalite is a hydrous ferrous ferric phosphate, the ferric analog of scorzalite. It is named in honor of A. L. de M. Barbosa, professor of geology, Escola de Minas, Minas Gerais, Brazil. The mineral occurs in black nearly opaque grains and masses that may be very fine grained aggregates. Thin grain edges are dark blue-green with evident pleochroism. The apparent mean index of refraction is 1.810, and the specific gravity is 3.60. The chemical analysis, recalculated to 100 percent after subtracting admixed tavorite, is FeO 13.12, MnO 2.82, Fe_2O_3 41.70, P_2O_5 37.54, and H_2O 4.92 percent. Its ideal chemical formula is $Fe^{II}Fe^{III}(PO_4)_2(OH)_2$. X-ray powder data indicate principal *d*-spacings at 3.361, 3.313, 4.84, 3.239, 3.160, and 2.327 A. The mineral is structurally identical with a synthesized compound described by Gheith as ferrous ferric lazulite and both are closely related to, but have a larger cell size than, scorzalite.

Tavorite and barbosalite are examples of complete substitution of trivalent iron for aluminum in known mineral structures.

M. L. LINDBERG
W. T. PECORA

U.S. Geological Survey
Washington 25, D.C.

Received April 27, 1954.

A Simplified Method for Determining Radioisotopes in Tissues

Several years ago, Schwebel, Isbel, and Karabinos [*Science* **113**, 465 (1951)] described a method for the measurement of C^{14} labeled carbohydrates, dissolved in pure foramamid; this served primarily as a medium of low vapor pressure usable in a modified flow gas counter. During a current study of the distribution in the body of a group of beta-emitting colloids (Au^{198}, $CrPo_4$, Y^{90}, it became necessary to have a method that would make possible rapid disintegration of entire organs of moderate-sized animals and of the entire bodies of smaller species. Formamid, even when hot, does not effect such solution directly, but we have found that when it is added to freshly prepared homogenates of animal tissues, a clear colloidal solution results even at room temperature. Such a solution may be rapidly liquid-counted at infinite thickness employing the usual end-window Geiger tube.

There is no need for prolonged acid or alkali digestion of tissues or evaporation of assay samples. As a result, there is a marked saving of time, and data can usually be completed on the same day the animals are sacrificed.

The method is equally applicable to gamma-emitters since the 50-percent formamid can be pipetted easily in the small volumes required for well types of scintillation tubes.

Organs that may be broken down in the Potter-Elvehjem homogenizer are so treated, in the presence of 10 to 100 ml H_2O. Larger samples and small animals are first broken up in a Waring Blendor, and a suitable aliquot put through the Potter-Elvehjem. We have found it advisable to pour, rather than pipette, 10-ml samples of this homogenate into graduates or volumetric flasks and to add an equal volume of formamid, with measurement in 30-ml beakers, at constant distance from the counting tube. An inexpensive and portable rate meter, such as the 1615 B, or a comparable instrument, has served adequately, and the direct readings again facilitate the running of a large num-

ber of samples. At the time of the animal injection, a duplicate sample of the colloid is prepared in water and serves as the standard for all subsequent measurements.

In case considerable skin is present, a small lump of hair will remain which may be filtered on cheesecloth and warmed with formamid; this procedure serves to extract any activity present. Since formamid is a good fat solvent, the presence of lipids does not present any problem. Only in the case of large bony structures is it necessary to resort to the much more cumbersome and hazardous HNO_3 digestion.

The method has been found to give values showing a strictly linear relation with respect to activity present. Standard deviations from average calculated values were ±2.2 percent for P^{32}, ±1.9 percent for Y^{90} and ±3.1 percent for Au^{198}.

A complete description of the method will appear in *Nucleonics*.

D. L. Tabern
T. N. Lahr

Abbott Laboratories, North Chicago, Illinois

Received January 11, 1954.

Mapping Shallow Horizons with the Reflection Seismograph

The reflection seismograph has long been the standard in geophysical exploration for oil, because some types of geologic structure can be mapped with this instrument with rather high precision. Until recently, however, the seismic reflection method has not been used in shallow structural and depth-to-bedrock investigations, partly because of instrumental difficulties and partly because the petroleum industry, which has provided the stimulus for improvement in seismic exploration, has been interested primarily in finding deep structures and stratigraphic traps. For shallower studies, in the depth range from the surface down to about 1000 ft, core drilling, the refraction seismograph, and electric-resistivity methods have been widely employed.

Reflection seismic instruments, specially constructed for the U.S. Geological Survey, have recently been successfully tested in two areas in Oklahoma and Kansas. Near Ponca City, Okla., in Osage County, the Neva limestone has been successfully mapped at a depth of about 200 ft. Near Lyons, in Rice County, Kan., the Stone Corral dolomite has been mapped at depths of 150 to 200 ft. In addition, the base of the overburden at a depth of less than 100 ft has been mapped in some places in the Kansas test area. Reflection times as small as 30 msec have been measured. In the Oklahoma test area, reflecting horizons have been mapped continuously from 200 ft to depths as great as 4000 ft. [For an example of shallow-reflection mapping at somewhat greater depths, see C. F. Allen, L. V. Lombardi, and W. M. Wells, *Geophysics* 17, 859 (1952)].

The instruments, designed by the Midwestern Geophysical Laboratory in close consultation with Survey geophysicists, are not radically different from conventional reflection seismic equipment. They have the following characteristics:

1) The frequency range of the 12 amplifiers is from 75 to 300 cy/sec (usually it is from 20 to 100 cy/sec).

2) The automatic volume-control time constant has been reduced to about a third of its usual value, and a variable presuppression control has been installed to permit a sharp reduction of the first energy arrivals.

3) The oscillograph paper speed has been increased from about 12 to 25 in./sec; high-frequency galvanometers have been installed, and the timing-line interval has been reduced from 10 to 2 msec.

The instruments can be used with or without automatic volume control and presuppression, and they are fully convertible to conventional operations by a simple amplifier exchange and a few oscillograph modifications. Reflected energy can be recorded almost immediately after the first arrivals.

In the Oklahoma test area, spread distances from the shot point of 100 to 210 ft between the first and twelfth geophones were used, and shots averaging 2 oz of dynamite were fired from shot holes drilled to the base of the "weathered" layer. A few single air shots were fired, but the record character was inferior to that for the hole shots. In the Kansas test area, spreads of from 20 to 130 ft were used with drilled shot holes and 2-oz charges (plus a few air shots in which the same disadvantage was displayed). No serious operational difficulties were encountered, although obtaining uniform amplitudes on each trace is less simple, because the travel distance for the first and last geophone positions is not as nearly identical as it is in conventional deep reflection work. Charge sizes are substantially smaller, and in some instances, with the automatic volume control and presuppression removed, a single blasting cap sufficed. The frequencies of recorded reflections averaged about 125 cy/sec.

Many of the limitations and ambiguities encountered in refraction work are absent in shallow-reflection mapping. The common refraction bugaboo of velocity inversion (the inability to detect low-velocity layers under high-velocity layers) is absent in the reflection method. Shallow-reflection work is much less expensive than core drilling, although some drilling for velocity and geologic control will always be necessary.

The shallow-reflection seismograph is expected to find wide application in ground-water and engineering investigations, mining investigations where stratigraphic and structural control of ore deposition is important, and in solving some of the near-surface problems in oil exploration. Both overburden-thickness problems and shallow structural problems in wide variety may be successfully solved by this new method.

L. C. Pakiser
D. R. Mabey

U.S. Geological Survey
Washington 25, D.C., and
Salt Lake City, Utah

Received April 27, 1954.

Mathematics and Federal Support

A QUESTION much discussed in scientific circles in Washington and in the universities is the level of Federal support of basic research in the sciences that is appropriate in terms of national policy and adequate in the view of research scientists. As new policies emerge in the Defense Department which seek to apply to all military programs the test of relevance to defense needs, it is not unnatural that particular concern should be felt (and expressed) by the mathematicians of the country about the fate they may expect for mathematics, and particularly for so-called "pure" mathematics.

It is still recognized in responsible military circles that a country strong scientifically must be strong mathematically. It is still clear that the total pattern of Federal support must provide adequate financing and broad and wise administration of funds. We are, however, in a period of reformulation of the details of policy.

One of the outcomes of our experiences in World War II was a commitment on the part of the Federal Government to the support of basic research. In 1946, this commitment found expression in the establishment of the Office of Naval Research. It was early decided as a matter of policy that sound support of mathematical research in this country must include support of work in pure mathematics. This policy still stands. But with the establishment of offices in the Army and the Air Force, also committed to the support of basic research, and with the emergence of the National Science Foundation as a civilian body with broad responsibility for maintaining and enhancing the scientific strength of the country, it has become necessary to restudy the shape of Federal support. The Foundation is concerned with all aspects of mathematical research and with related problems of mathematical manpower at all levels. It is natural that, in mathematics, it should support an outstanding program in some of the more abstract fields, where much of the most significant research is going on. Recognizing this, ONR has planned for gradual withdrawal from some of these fields, while maintaining a strong program in analysis and in various less abstract fields. But this withdrawal has always been conditioned by ONR's continuing concern that the total support for mathematics provided by Federal agencies should be maintained in such a way and at such a level that the Navy's long term needs would be adequately served. The Office of Ordnance Research of the Army and the Office of Scientific Research of the Air Force also initiated vigorous mathematics programs; and these continue.

In the course of the last 2 years, the funds provided for research in abstract mathematics by the National Science Foundation have been slightly less than the funds withdrawn from these fields by ONR; but fellowships and conferences have won support greater than that provided by ONR for comparable purposes (ONR had no fellowship program—but certain contracts did provide for the individual research of exceptionally promising young mathematicians). The Army and the Air Force have maintained such strong programs that the total funds for mathematical research have not been reduced. Although the future of military contracts is not clear, a vigorous effort is being made to preserve adequate financing of mathematical research within the military budget.

Responsibility for initinting and defending policy with respect to the support of mathematics within the three military departments is shared by the mathematicians working in these departments; and they, together with the mathematics staff of the National Science Foundation, are trying in the most serious and intelligent way to use the funds and other resources at their disposal to secure a continuation of the lively and significant development of mathematical research that has characterized the postwar era. The responsible leaders of the mathematical community are giving them needed help in this effort; but the position of mathematics would be greatly strengthened by a clearer presentation by mathematicians of the needs of mathematics.

MINA REES
Chairman, Section A, AAAS
Hunter College, New York

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TRAVEL ARRANGEMENTS FOR THE AAAS BERKELEY MEETING

December 26-31, 1954

In time or in cost, a trip from an eastern city to California is not much more than a **round trip** to a midwestern city. Californians who for years have been attending meetings in the East have told their colleagues that the continental distance is the **same** each way, and that it should be the turn of the Easterners to visit the Pacific Coast.

The Association is planning ways it may assist those who will attend the 121st AAAS Meeting on the campus of the University of California at Berkeley, this December. The possibilities include:

1. Low cost AAAS limousines from Oakland and San Francisco airports and railroad terminals direct to the dormitory or hotel of each delegate.
2. Arrangements for traveling together in AAAS cars on fast trains leaving Chicago, Washington, D. C., and New York.
3. Arrangements for chartering first class DC6, 6B, or 7 planes of scheduled airlines—at prices comparable with air coach travel.

Note: In the following table of **round-trip** fares all figures include the new lowered 10% federal tax.

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Reclining seat coach	$ 99.17	$147.62	$156.64
First class	$139.10	$204.33	$222.67
Lower berth	46.20	60.06	63.58
Total	$185.30	$264.39	$286.25
By Air	Time: 7–8 hrs., leaving a.m. or p.m., Dec. 26; returning a.m. or p.m. Dec. 31	Time: 10–11 hrs., leaving a.m. or p.m., Dec. 26; returning a.m. or p.m., Dec. 31	Time: 10–11 hrs., leaving a.m. or p.m., Dec. 26; returning a.m. or p.m., Dec. 31
Air coach (no meals)	$167.20	$215.60	$217.80
Chartered 1st class (meals included)	c. $178.00	c. $235.00	c. $235.00
First class (meals included)	$239.91	$312.18	$332.09

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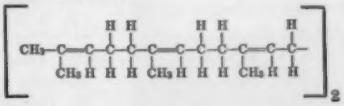
Lens movie

We have had a composer compose some original music for us. *Why?* To serve as background for a movie. *Are we in the business of producing movies with music in them to entertain people?* No, but the right kind of music in a movie helps hold people's interest while they learn. *Learn what?* Most anything. About photographic lenses, in this particular case. *What about photographic lenses?* About how they are designed and how the glass is made and how the blocking, grinding, polishing, centering, coating, mounting, finishing, and testing are done. *Who cares?* Several different classes of people care about 25 minutes' worth, we hope. For examples: 1) youngsters with a healthy curiosity about the various basic technologies that underlie our civilization; 2) engineers and businessmen sufficiently catholic in their interests to realize that it often pays to watch over another fellow's shoulder if he's willing and seems to know what he is doing; 3) professional photographers and amateur camera fans who want to see how good lenses are made. *How is this film booked for showing?* By a note to Eastman Kodak Company, Camera Club and School Service, Rochester 4, N. Y., to give us an idea of what folks will be in the audience and what organization will assume responsibility for sending the film back to us in good shape. The title is "Quality in Photographic Lenses." There is no rental charge.

Fascinating hydrocarbon

Strung up here is a *basking* shark, so called because the non-pregnant female of the species loves to lie near the surface and bask, exposing the tip of her nose, her dorsal fin, and the top of her tail. Sometimes more than 30 feet in length and 4½ tons in weight, it is larger than any land animal.

Its gigantic liver drips with an oil that is poor in vitamin A but contains some 30 per cent of a fascinating hydrocarbon, *Squalene*, with this structure:



We wish to advise that we have procured a quantity of basking shark liver oil and have molecularly distilled from it a colorless, high-boiling cut which is 90-95% *Squalene*, and now offer this in the market place as Eastman Organic Chemical No. P6966 at $2 for 100 grams, $8 for 500 grams. On a really big deal you might succeed in bargaining us down considerably. Like all Eastman Organic Chemicals, it is presently available only on assurance of no use or resale as a food or drug ingredient. It is for investigational use only.

About this deceptively simple isoprene polymer there appears to be plenty to investigate, aside from the riddle of why the basking shark and the cacao shark of East African waters accumulate so much of it. Its presence in olive oil and absence from vegetable oils likely to be palmed off as olive oil arouses the investigational instincts of law enforcement bodies. It is a precursor of cholesterol. Though it is a normal component of human sebum, in topical application it is reported to cause loss of hair without signs of inflammation. (Unfortunately, a consulting firm we hired to check this observation failed to confirm it.) Somehow *Squalene* stimulates controversy. Several short notes have appeared in the literature about "regenerated squalene," the product obtained by recovery from the hexahydrochloride. It appears that here a considerable number of the double bonds have shifted so that some of the methyl groups have changed to methylenes. This product, therefore, is quite different from natural squalene.

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Meetings & Conferences

June

20–22. Conf. on Liquid Structure and Acoustics, Providence, R.I. (R. B. Lindsay, Dept. of Physics, Brown Univ., Providence.)

20–23. American Astronomical Soc., Ann Arbor, Mich. (C. M. Huffer, Washburn Observatory, Madison 6, Wis.)

20–23. American Soc. of Agricultural Engineers, annual, Minneapolis, Minn. (F. B. Lanham, ASAE, St. Joseph, Mich.)

20–24. American Soc. of Medical Technologists, Miami Beach, Fla. (R. Matthaei, Suite 25, Hermann Professional Bldg., Houston 25, Tex.)

20–25. American Inst. of Chemical Engineers, Ann Arbor, Mich. (D. L. Katz, Dept. of Chemical Engineering, Univ. of Michigan, Ann Arbor.)

20–25. American Soc. of Mechanical Engineers, semiannual, Pittsburgh, Pa. (C. E. Davies, 29 W. 39 St., New York.)

20–25. International Meeting on Chemical Engineering Aspects of Nuclear Processes, Ann Arbor, Mich. (D. L. Katz, Dept. of Chemical Engineering, Univ. of Michigan, Ann Arbor.)

20–26. American Library Assoc., annual, Minneapolis, Minn. (D. H. Clift, 50 E. Huron St., Chicago 11, Ill.)

20–10. National Training Laboratory in Group Development, Bethel, Me. (L. P. Bradford, 1201 16 St. NW, Washington 6, D.C.)

21–23. Chemical Inst. of Canada, 37th annual, Toronto, Can. (D. W. Emmerson, 18 Rideau St., Ottawa 2.)

21–24. Agricultural Inst. of Canada and Canadian Phytopathological Soc., annual, Macdonald College, Canada. (A. J. Skolko, Div. of Botany and Plant Pathology, Central Exptl. Farm, Ottawa, Ont.)

21–25. Alpha Chi Sigma Fraternity, annual, East Lansing, Mich. (J. R. Kuebler, 5503 E. Washington St., Indianapolis 19, Ind.)

21–25. American Inst. of Electrical Engineers, summer general and Pacific general, Los Angeles, Calif. (H. H. Henline, 33 W. 39 St., New York 18.)

21–25. Ecological Soc. of America, western section, Pullman, Wash. (J. W. Marr, Dept. of Biology, Univ. of Colorado, Boulder.)

21–25. Symposium on Impact of Solid State Science on Engineering Materials, Pittsburgh, Pa. (J. W. Graham, Jr., College of Engineering, Carnegie Inst. of Technology, Pittsburgh 13.)

21–25. Technical Writers' Inst., 2nd annual, Troy, N.Y. (J. R. Gould, Rensselaer Polytechnic Inst., Troy.)

21–25. American Medical Assoc., annual, San Francisco, Calif. (AMA Office, 535 N. Dearborn St., Chicago 10.)

21–26. American Assoc. for the Advancement of Science, Pacific Division, Pullman, Wash. (R. C. Miller, California Acad. of Science, Golden Gate Park, San Francisco 18.)

22–24. American Dairy Science Assoc., 49th annual, State College, Pa. (J. O. Almquist, College of Agriculture, Pennsylvania State Univ., State College.)

22–24. Oceanographic Convocation, Woods Hole, Mass. (H. R. Gault, National Research Council, Washington 25, D.C.)

23–25. Cong. for the Advancement of Spectrographic Methods, 17th, Paris, France. (Sec., G.A.M.S., 1, Place St. Thomas d'Aquin, Paris 7.)

23–26. Acoustical Soc. of America, 25th, New York, N.Y. (W. Waterfall, 57 E. 55 St., New York 22.)

Meetings & Conferences

June, *contd.*

25–29. Inst. of Aeronautical Sciences, New York, N.Y. (S. P. Johnston, 2 E. 64 St., New York.)

27–1. Inst. of Food Technologists, annual, Los Angeles, Calif. (C. S. Lawrence, 176 W. Adams St., Chicago 3, Ill.)

28–29. National Science Teachers Assoc., New York N.Y. (R. H. Carleton, 1201 16 St. NW, Washington 6, D.C.)

28–30. American Assoc. of Physics Teachers, Minneapolis, Minn. (R. F. Paton, Univ. of Illinois, Urbana.)

28–30. American Physical Soc., Minneapolis, Minn. (K. K. Darrow, Columbia Univ., New York 27.)

28–30. American Soc. of Heating and Ventilating Engineers, 60th semiannual, Swampscott, Mass. (Sec., ASHVE, 62 Worth St., New York 13.)

28–2. European Cong. of Gastroenterology, 4th, Paris, France. (A. Busson, 63 bis Rue de Varenne, Paris 7.)

28–3. National Education Assoc., annual, New York, N.Y. (L. W. Ashby, 1201 16 St. NW, Washington, D.C.)

29–3. International Conf. on Semiconductors, Amsterdam, The Netherlands. (H. J. Vink, Floralaan 142, Eindhoven, Netherlands.)

30–2. Heat Transfer and Fluid Mechanics Inst., Berkeley, Calif. (H. A. Johnson, Dept. of Mechanical Engineering, Univ. of California, Berkeley.)

July

1–9. British Medical Assoc., Glasgow, Scotland. (BMA, Tavistock Square, London, WC 1.)

2–8. International Cong. of Oto-Neuro-Ophthalmology, 19th, São Paulo, Brazil. (C. de Rezende, Hospital das Clinicas, Avenida Ademar de Barros, São Paulo.)

2–14. International Cong. of Botany, 8th, Paris, France. (P. Chouard, 11, Rue de Val-de-Grace, Paris 5.)

6–9. American Home Economics Assoc., San Francisco, Calif. (Miss M. Horton, 1600 20 St. NW, Washington, D.C.)

7–10. American Physical Soc., Seattle, Wash. (J. Kaplan, Univ. of California, Los Angeles.)

8–9. International Union of Pure and Applied Physics, 8th, London, Eng. (H. A. Barton, 57 E. 55 St., New York 22.)

8–13. Conv. on Industrial Electronics, Oxford, Eng. (Sec., Brit. I.R.E., 9 Bedford Sq., London, W.C.1.)

10–15. Latin American Cong. on Gynecology and Obstetrics, 2nd, São Paulo, Brazil. (J. Ramos, Av. Brigadeiro Luiz Antonio, 278–80, São Paulo.)

11–14. American Soc. of Refrigerating Engineers, Seattle, Wash. (M. C. Turpin, 234 5 Ave., New York 1.)

13–17. Conf. on Defects in Crystalline Solids, Bristol, Eng. (H. A. Barton, 57 E. 55 St., New York 22.)

13–17. Cong. on Experimental and Theoretical Nuclear Physics, Glasgow, Scotland. (H. A. Barton, 57 E. 55 St., New York 22.)

15–17. International Symposium on Solid Particles in Astronomical Objects, Liége, Belgium. (P. Th. Oosterhoff, Leiden Observatory, Leiden, Netherlands.)

15–21. Pan American Cong. of Child Welfare and Pediatrics, 4th, São Paulo, Brazil. (J. Ramos, Av. Brigadeiro Luiz Antonio 278–80, São Paulo.)

16–21. International Conf. on Electron Microscopy, London, Eng. (F. W. Cuckow, Royal Cancer Hospital, London, SW 3.)

Meetings & Conferences

July, *contd.*

17–22. Latin American Cong. on Mental Health, 1st, São Paulo, Brazil. (A. C. Pacheco e Silva, Av. Brigadeiro Luiz Antonio 278–80, São Paulo.)

19–23. International Cong. of Gerontology, 3rd, London and Oxford, Eng. (Mrs. A. Humpage, Tavistock Square, London, WC 1.)

19–24. Pan American Cong. on Gastroenterology, 5th, São Paulo, Brazil. (J. Ramos, Av. Brigadeiro Luiz Antonio 278–80, São Paulo.)

20–24. International Conf. on Thrombosis and Embolism, Basel, Switzerland. (W. Merz, Gynecological Clinic, Univ. of Basel.)

21–24. International Cong. of Medical Psychotherapy, Zurich, Switzerland. (H. K. Fiers-Monnier, Hauptstrasse 8, Kreuzlingen, Switzerland.)

21–28. International Cong. of Crystallography, 3rd, Paris, France. (J. D. H. Donnay, Johns Hopkins Univ., Baltimore, Md.)

23–29. International Cancer Cong., 6th, São Paulo, Brazil. (H. L. Stewart, National Cancer Inst., Bethesda, Md.)

25–31. Inter-American Cong. of Sanitary Engineering, 4th, São Paulo, Brazil. (L. Nogueira, Caixa Postal 8099, São Paulo.)

26–31. International Cong. of Gynecology and Obstetrics, Geneva, Switzerland. (W. Geisendorf, Maternite, Hôpital Cantonal, Geneva.)

27–28. International Union of Theoretical and Applied Mechanics, 4th, Brussels, Belgium. (H. L. Dryden, 1724 F St. NW, Washington 25, D.C.)

28–2. International Union for the Protection of Nature, 4th, Copenhagen, Denmark. (H. J. Coolidge, National Research Council, Washington 25, D.C.)

28–2. Symposium on Photoelasticity and Photoplasticity, Brussels, Belgium. (H. L. Dryden, 1724 F St. NW, Washington 25, D.C.)

August

1–2. Linguistic Soc. of America, Chicago, Ill. (A. A. Hill, 1719 Massachusetts Ave., NW, Washington 6, D.C.)

3–13. Pan American Federation of Engineering Societies, 3rd, São Paulo, Brazil. (H. Pegado, Edificio Maua, Viaduto Dona Paulina, São Paulo.)

9–27. Summer Seminar in Statistics, 5th, Storrs, Conn. (G. Beall, Dept. of Statistics, Univ. of Connecticut, Storrs.)

10–14. Canadian Teachers' Federation, annual, Vancouver, Canada. (G. G. Croskery, 444 Mac Laren St., Ottawa.)

12–14. International Cong. on Group Psychotherapy, 1st, Toronto, Can. (J. L. Moreno, 101 Park Ave., New York 17.)

13–14. International Cong. on Child Psychiatry, Toronto, Can. (A. Z. Barhash, 186 Clinton Ave., Newark 5, N.J.)

13–21. World Poultry Cong., 10th, Edinburgh, Scotland. (Cong. Sec., Dept. of Agriculture for Scotland, St. Andrew's House, Edinburgh 1.)

14–21. International Cong. on Mental Health, 5th, Toronto, Can. (J. D. Griffin, 111 St. George St., Toronto 6.)

15–28. Pan Indian Ocean Science Cong., Perth, Western Australia. (A. D. Ross, 31 Ventnor Ave., West Perth.)

Meetings & Conferences

August, *contd.*

19–20. National Council of Geography Teachers, San Francisco, Calif. (Mrs. I. C. Robertson, State Teachers College, Valley City, N.D.)

19–31. International Conf. of Ship Hydrodynamics, 7th, Göteborg, Sweden. (H. F. Nordstrom, Statens Skeppsprovningsanstalt, Göteborg.)

20–26. American Pharmaceutical Assoc., Boston, Mass. (R. P. Fischelis, 2215 Constitution Ave., NW, Washington 7, D.C.)

23–26. American Veterinary Medical Assoc., annual, Seattle, Wash. (J. G. Hardenbergh, 600 S. Michigan Ave., Chicago 5, Ill.)

23–28. International Cong. for the Philosophy of Science, 2nd, Zurich, Switzerland. (Sec., Internationales Forum Zurich, Room 20d, Eidengenssische Hochschule, Zurich 6.)

23–28. International Cong. of Soil Science, 5th, Leopoldville, Belgian Congo. (F. A. van Baren, Royal Tropical Inst., Mauritskade 63, Amsterdam, Netherlands.)

23–28. International Photobiological Cong., Amsterdam, Netherlands. (Cong. Sec., Radiologische Laboratorium, Wilhelminagasthuis, Amsterdam.)

23–3. International Scientific Radio Union, 11th, The Hague, Netherlands. (I. E. Herbays, 42 Rue des Minimes, Brussels, Belgium.)

25–27. American Phytopathological Soc., annual, Estes Park, Colo. (G. S. Pound, Dept. of Plant Pathology, Univ. of Wisconsin, Madison.)

25–27. Western Electronics Show and Convention, Los Angeles, Calif. (M. Mobley, Jr., 344 N. LaBrea Ave., Los Angeles 36.)

30–31. Mathematical Assoc. of America, 35th summer, Laramie, Wyo. (H. M. Gehman, Univ. of Buffalo, Buffalo 14, N.Y.)

30–1. American Soybean Assoc., 34th annual, Memphis, Tenn. (G. M. Strayer, ASA office, Hudson, Iowa.)

30–3. International Soc. of Orthopedic Surgery and Traumatology, 6th, Bern, Switzerland. (M. Dubois, Isle-Hospital, Bern.)

30–3. International Symposium on Combustion, 5th, Pittsburgh, Pa. (B. Lewis, Alcoa Bldg., Pittsburgh 19.)

30–9. International Mathematical Cong., Amsterdam and The Hague, Netherlands. (M. H. Stone, Dept. of Mathematics, Univ. of Chicago, Chicago 37, Ill.)

31–3. American Mathematical Soc., summer, Laramie, Wyo. (E. G. Begle, AMS, Yale Univ., New Haven, Conn.)

31–10. World Population Cong., Rome, Italy. (F. Lorimer, American Univ., Washington 16, D.C.)

September

1–7. International Soc. for Cell Biology, 8th, Leiden, Netherlands. (W. H. K. Karstans, Botanical Laboratory, State University, Nonnensteig 3, Leiden.)

1–8. British Assoc. for the Advancement of Science, annual, Oxford, England. (Sec., BAAS, Burlington House, London, W.1.)

1–8. International Cytological Cong., Leiden, Netherlands. (P. G. Gaillard, Histologisch Laboratorium, Rijksuniversiteit, Leiden.)

1–11. International Committee of Electrochemical Thermodynamics and Kinetics, 6th annual, Paris and Poitiers, France. (P. Van Rysselberghe, Dept. of Chemistry, Univ. of Oregon, Eugene.)

Meetings & Conferences

September, contd.

1–16. International Electrotechnical Commission, 50th, Philadelphia, Pa. (U.S. Committee, American Standards Assoc., 70 E. 45 St., New York 17.)

2–9. International Cong. of Mathematicians, annual, Amsterdam, Netherlands. (Sec., 2d Boerhaavestraat 49, Amsterdam.)

3–7. International Symposium on Infrared, Parma, Italy. (S. S. Ballard, The Rand Corp., Santa Monica, Calif.)

3–8. American Psychological Assoc., annual, New York City. (F. H. Sanford, 1333 16 St., NW, Washington 6, D.C.)

3–8. Psychometric Soc., annual, New York City. (J. B. Carroll, Harvard Univ., 13 Kirkland St., Cambridge 38, Mass.)

5–9. American Inst. of Biological Sciences, Gainesville, Fla. (F. L. Campbell, 2101 Constitution Ave., Washington, D.C.)

5–9. American Bryological Soc., Gainesville, Fla. (L. J. Gier, Dept. of Biology, Wm. Jewell College, Liberty, Mo.)

5–9. American Fern Soc., Gainesville, Fla. (W. H. Wagner, Dept. of Botany, Univ. of Michigan, Ann Arbor.)

5–9. American Soc. for Horticultural Science, Gainesville, Fla. (F. S. Howlett, Ohio Agricultural Experiment Station, Wooster.)

5–9. American Soc. of Human Genetics, Gainesville, Fla. (S. C. Reed, Univ. of Minnesota, Minneapolis 14.)

5–9. American Soc. of Ichthyologists and Herpetologists, Gainesville, Fla. (A. Grobman, Dept. of Biology, Univ. of Florida, Gainesville.)

5–9. American Soc. of Limnology and Oceanography, Gainesville, Fla. (B. H. Ketchum, Woods Hole Oceanographic Institution, Woods Hole, Mass.)

5–9. American Soc. of Naturalists, Gainesville, Fla. (W. S. Spencer, Dept. of Biology, Wooster College, Wooster, Ohio.)

5–9. American Soc. of Plant Physiologists, Gainesville, Fla. (J. F. Stanfield, Miami Univ., Oxford, Ohio.)

5–9. American Soc. of Plant Taxonomists, Gainesville, Fla. (R. C. Rollins, Gray Herbarium, Harvard Univ., Cambridge 38, Mass.)

5–9. Biometric Soc. ENAR, Gainesville, Fla. (A. M. Dutton, Box 287, Station 3, Rochester 20, N.Y.)

5–9. Botanical Soc. of America, Gainesville, Fla. (H. B. Creighton, Dept. of Botany, Wellesley College, Wellesley 81, Mass.)

5–9. Ecological Soc. of America, Gainesville, Fla. (J. F. Reed, Dept. of Botany, Univ. of Wyoming, Laramie.)

5–9. Genetics Soc. of America, Gainesville, Fla. (C. P. Oliver, Dept. of Zoology, Univ. of Illinois, Urbana.)

5–9. Mycological Soc. of America, Gainesville, Fla. (L. Shanor, Dept. of Botany, Univ. of Illinois, Urbana.)

5–9. National Assoc. of Biology Teachers, Gainesville, Fla. (J. P. Harrold, 110 E. Hines St., Midland, Mich.)

5–9. The Nature Conservancy, Gainesville, Fla. (G. B. Fell, 607 G St., SE, Washington 3, D.C.)

5–9. Phi Sigma Soc., Gainesville, Fla. (F. S. Orcutt, Dept. of Biology, Virginia Polytechnic Inst., Blacksburg.)

5–9. Sigma Delta Epsilon, Gainesville, Fla. (M. Gojdics, Barat College, Lake Forest, Ill.)

5–9. Soc. of Protozoologists, Gainesville, Fla. (N. D. Levine, College of Veterinary Medicine, Univ. of Illinois, Urbana.)

Miscellaneous Publications

Absorption Coefficients of Several Atmospheric Gases. Geophysical Research Papers No. 21, AFCRC Tech. Rpt. 53–23. K. Watanabe, Murray Zelikoff, and Edward C. Y. Inn. 80 pp. Illus. ***Asymptotic Approximation for the Elastic Normal Modes in a Stratified Solid Medium.*** G.R.P. No. 22, Tech. Rpt. 53–27. Norman A. Haskell. 23 pp. Illus. ***Forecasting Relationships between Upper Level Flow and Surface Meteorological Processes.*** G.R.P. No. 23, Tech. Rpt. 53–28. J. J. George *et al.* 186 pp. Illus. Geophysics Research Directorate, Air Force Cambridge Research Center, Cambridge 38, Mass., 1953. Free on application to U.S. Dept. of Commerce, Office of Technical Services, Washington 25, D.C.

The Acanthaceae of Colombia, II. Contributions from the U.S. National Herbarium. Vol. 31, Pt. 2, 1953. Emery C. Leonard (Order from Supt. of Documents, GPO, Washington 25, D.C.). 322 pp. Illus. 70¢.

Annual Epidemiological and Vital Statistics, 1947–1949. Pt. II: ***Cases of and Deaths from Notifiable Diseases*** (In English and French). World Health Organization, 1953 (Order from Columbia Univ. Press, New York 27). 291 pp. $3.75.

The Application of Dyes to Textile Fibers at High Temperatures. Calco Tech. Bull. No. 833. Charles L. Zimmerman. American Cyanamid Co., Bound Brook, N.J., 1953. 16 pp. Illus. Free.

Auxiliaries for Wool Processing. Antara Chemicals, 435 Hudson St., New York 14, 1953. 46 pp. Free.

Britain's Atomic Factories. The story of atomic energy production in Britain. K. E. B. Jay. Her Majesty's Stationery Office, London, 1954 (U.S. distr.: British Information Services, 30 Rockefeller Plaza, New York 20). 100 pp. Illus. + plates. 5s.

Causes of Public Unrest Pertaining to Education. Ser. I, No. 56 (Extracts from the 1953 Harvard Summer School Conference on Educational Administration). Raymond F. Howes, Ed. American Council on Education, Washington 6, D.C., 1953. 74 pp. $1.

Chemistry and Chemical Engineering at the California Institute of Technology. A report for the year 1952–1953 on the research and other activities of the Division of Chemistry and Chemical Engineering. California Institute of Technology, Pasadena 4, Calif., 1953. 121 pp. Illus.

Collected Papers with Summarised Account of Contents. Vol. X (Animal nutrition). Rowett Research Institute, Bucksburn, Aberdeenshire, Scotland, 1954. 23 pp. 2s 6d.

Commercial Feeding Stuffs, Report on Inspection, 1952. Bull. 573. H. J. Fisher. Connecticut Agricultural Expt. Station, New Haven, 1953. 116 pp.

The Commercial Fish Catch of California for the Year 1952. Fish Bull. No. 95. California State Fisheries Laboratory, Terminal Island Station, San Pedro, 1954. 68 pp. Illus. Free.

Desert Research. Proceedings of the international symposium held in Jerusalem, May 7–14, 1952, sponsored by Research Council of Israel and UNESCO. Spec. Pub. No. 2. Research Council of Israel, Jerusalem, 1953 (Order from Interscience Pub., New York 1). 641 pp. Illus. $6.

Expert Committee on Mental Health. Third Report, 1953. Tech. Rpt. Ser., No. 73. 38 pp. 25¢. ***Expert Committee on Plague.*** Second Report. Tech. Rpt. Ser., No. 74. 13 pp. 10¢. World Health Organization, Geneva, 1953.

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